Correlation of tear film-specific immunoglobulin E assay with the skin prick test in allergic conjunctivitis

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Received 17 April 2017
Accepted 1 July 2017

Delta Journal of Ophthalmology
2017, 18:123–132

Purpose
The aim of this study was to investigate the correlation and validity of tear film allergen-specific immunoglobulin E (IgE) in relation to the skin prick test in diagnosing different types of allergic conjunctivitis.
Design
The study design was a prospective randomized case series.
Patients and methods
One hundred and twenty patients with allergic conjunctivitis were included in this study and were classified into four groups according to the type of allergy.
Group 1 included 48 patients with perennial allergic conjunctivitis. Group 2 included 35 patients with seasonal allergic conjunctivitis. Group 3 included 30 patients with vernal keratoconjunctivitis (VKC), and group 4 included seven patients with atopic keratoconjunctivitis. All patients were subjected to the skin prick test, which was performed with aeroallergen panel using kits containing different inhalant allergens, positive control (histamine 1 mg/ml), and negative control (saline 0.9%). Tear samples were collected using the microcapillary method for the quantitative determination of specific IgE using immune blot assay. Data were evaluated and statistically analyzed.
Results
In this study, the skin prick test and specific IgE were performed to 11 different allergens and the results revealed that the most common mixed allergens were mixed pollen, mixed mould, and mixed mite. Validity of tear film-specific IgE in the detection of allergens was assessed against the skin prick test (gold standard). There was IgE specificity of 100%, whereas the sensitivity ranged from 50 to 100% to the three common allergens in the four groups. There was a statistically significant correlation between specific IgE and the skin prick test for the most common allergens in patients with perennial allergic conjunctivitis, seasonal allergic conjunctivitis, and VKC (except for mould allergens in the VKC group). There was only a statistically significant correlation between specific IgE and the skin prick test for mite allergen in patients with atopic keratoconjunctivitis.
Conclusion
Tear film-specific IgE has a statistically significant correlation and validity when compared with the skin prick test in diagnosing the causative allergen in different types of allergic conjunctivitis. It could be a good alternative to the skin prick test in the diagnosis of allergic conjunctivitis with high sensitivity and specificity and fewer complications and limitations.

Keywords:
allergic conjunctivitis, skin prick test, specific immunoglobulin E, tear film

DJO 18:123–132

1110-9173

Introduction

Conjunctivitis, accounting for 14% of all eye diseases, is considered one of the most common eye diseases in general ophthalmic practice. Its causes include infections with bacteria and viruses, and allergic conjunctivitis [1].

The prevalence of ocular allergies is estimated to be over 20% in the USA and 18% in the UK [2].

Allergic conjunctivitis could be categorized as seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis (PAC), vernal keratoconjunctivitis (VKC), and atopic keratoconjunctivitis (AKC) [3]. A proper etiological diagnosis of allergic conjunctivitis will result in consequent efficacious treatment. This justifies close cooperation between two specialists, ophthalmologists, and allergists to achieve this goal.

Diagnosis of an allergic disease is principally based on history and clinical examination, and can be confirmed

 DOI: 10.4103/DJO.DJO_30_17

by means of skin prick tests (SPT) or measurement of antigen-specific immunoglobulin E (IgE) levels [4–6]. Specific IgE-mediated allergic reactivity can simply be tested for using either an in-vivo SPT or an in-vitro enzyme or fluorescence-based immunoassay, commonly called a radioallergosorbent test [7].

Numerous epidemiologic studies have verified strong associations among serum IgE levels and skin test reactivity to different allergens, yet the details of these relations are still not clear [8–11].

Allergen-specific IgE testing is commonly used in the diagnosis of IgE-mediated atopic diseases, but there is still a debate about the relative value of in-vitro measurement of IgE antibody in comparison with in-vivo skin tests [12].

This study was planned to investigate the correlation and validity of tear film allergen-specific IgE in relation to the SPT in different types of allergic conjunctivitis.

Patients and methods

This study was carried out between May 2016 and January 2017.

The study was approved by the Local Ethical Committee of Zagazig University. Written consent was obtained from the patients and included an explanation of the study.

This is a randomized prospective study to correlate and assess the validity of tear film-specific IgE assay in relation to the SPT in allergic conjunctivitis.

One hundred and forty-eight patients with suspected allergic conjunctivitis (history of itching, red eye, swollen eyelids, foreign body sensation, and lacrimation) were examined with a slit lamp biomicroscopy for confirmation of the diagnosis of allergic conjunctivitis and for determination of its type. The exclusion criteria were viral conjunctivitis, bacterial conjunctivitis, giant papillary conjunctivitis, and toxic conjunctivitis.

Classification of allergic conjunctivitis was carried out after clinical examination and history taking as follows.

Seasonal allergic conjunctivitis

Diagnostic aspects of SAC consist of itching, redness, and chemosis. Redness, or conjunctival injection, tends to be mild to moderate, whereas chemosis is usually moderate, and itching is a somewhat constant symptom of SAC. However, corneal involvement is rare [13].

Airborne pollens are usually the causative allergens in SAC. Manifestations usually occur in summer and spring, and lessen in the winter months [13].

Perennial allergic conjunctivitis

Diagnostic features of SAC and PAC are similar, but the allergens to which the patient is allergic are different. In PAC the allergens are present throughout the year and the allergy is perennial with exposure to these allergens [13].

Vernal keratoconjunctivitis

VKC has three clinical forms, palpebral, limbal, and mixed, with an overall majority in male population. Young people are usually affected. Symptoms include ocular itching, redness, swelling, and discharge. Itching may be very severe. Patients have frequently photophobia, sometimes quite severe. The most characteristic sign is giant papillae (cobblestone-like swellings) on the upper tarsal conjunctiva, usually 10–20 in number [14].

The cornea may be affected in VKC. A punctate keratitis can occur and may coalesce to form an opacity. This frequently leads to a grayish or whitish subepithelial plaque. Trantas dots may be seen at the limbus [13].

Atopic keratoconjunctivitis

Eczematous skin lesions (red and elevated) are characteristic and may be found on the eyelids, or any place on the body. Ocular findings vary. There may be mild-to-severe chemosis and conjunctival injection. Conjunctival scarring is familiar. Trantas dots, giant papillae may also be present and cataracts may also occur in AKC [15].

One hundred and twenty patients met the inclusion criteria and provided informed consent. These patients were classified into four groups according to the type of allergy as follows: group 1included patients with PAC; group 2 included patients with SAC; group 3 included patients with VKC; group 4 included patients with AKC.

The patients' demographic data, clinical data, and history were recorded.

The patients were instructed to avoid antihistamines (first generation: 3 days; second generation: 5 days), systemic corticosteroids (6 days), and mast cell stabilizers (2 days)

before testing, as these medications can affect the interpretation of both the SPT and IgE assay.

All patients were subjected to the following: SPT, tear sampling, and measurement of tear-specific IgE.

Skin prick test

A routine SPT was performed with aeroallergen panel using kits containing different inhalant allergens, negative control (saline 0.9%), and positive control (histamine 1 mg/ml).

The kit of aeroallergen panel includes the following inhalant allergens supplied in 5 ml vials (Omega Laboratory, Montreal, Canada): mixed pollen (grass, birch, and ragweed), mixed mould (*Aspergillus fumigatus*, *Aspergillus niger*, and *Alternaria* spp.), mixed mite (*Dermatophagoides pteronyssinus* and *Dermatophagoides farina*), *Candida albicans*, dog epithelium, cat epithelium, feather mix, cockroach, hay dust, house dust, and smoke.

A drop of solution of each test allergen and control was placed on the flexor surface of the forearm, and skin was pricked at the drop midpoint.

SPT was considered positive if the induration was larger than the control by 3 mm or more after 15 min. A larger wheal means greater allergic response [16].

The reactions were recorded in accordance with the recommendations of the Standardization Committee of the Northern Society of Allergology, as shown in Table 1 [17].

Tear sampling

The microcapillary method (Fig. 1) was used to collect tear samples from the temporal side of tear meniscus without local anesthesia. The patient was asked to look in the opposite direction during sampling and not to blink [18].

Measurement of tear-specific immunoglobulin E

Immune blot assay was used for the quantitative determination of specific IgE in tear samples against aeroallergen (same allergens used in the SPT) and antigoat IgG as positive control with Allergy Screen Panel 2A EGY (MEDIWISS Analytic GmbH, Hanover, Germany) according to the manufacturer's instructions. Briefly, the tears were pipetted into a trough of nitrocellulose membrane coated with specific allergens, followed by addition of biotin-coupled anti-human IgE antibody, streptavidin conjugated with alkaline phosphatase, and substrate, in order. The color reaction of each precipitate line on the test trough indicated specific antibody content. Tear-specific IgE was analyzed with Rapid Reader (Improvio, Germany) using the densitometer curve of the membrane and concentration data for each intensity. The result was expressed in IU/ml and classified into six classes (Table 2) reflecting allergen-specific IgE content of the tears according to the manufacturer's instructions. The test was valid if positive control IgE was more than 3.5 IU/ml.

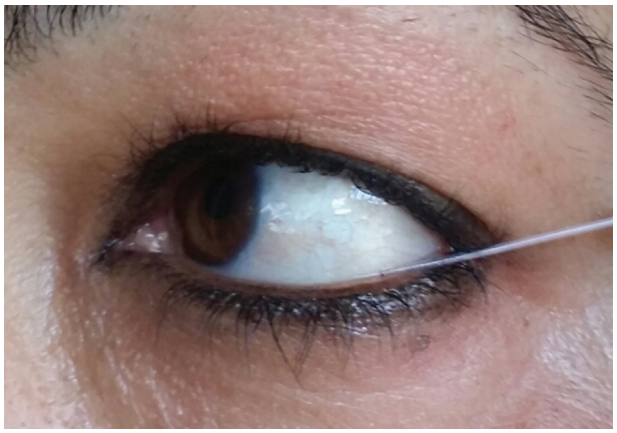
Statistical analysis

The collected data were coded and analyzed with computer using a database software program, statistical package for the social sciences, version 19 (SPSS Inc., IBM Company, New York, USA).

Table 1 Grading of the skin prick test

Grades	Wheal size
0	No reaction
1	1/3 of positive control
2	1/2 to 2/3 of positive control
3	Same as positive control
4	Larger than positive control
5	Pseudopod (irregular wheal)

Figure 1



Micro capillary method used to collect tear samples.

Table 2 Relationship between the classes found and allergen-specific immunoglobulin E content

Classes	IgE level (IU/ml)	Allergen-specific IgE
Class I	0.35–0.69	Low
Class II	0.7–3.4	Increased
Class III	3.5–17.4	Significantly increased
Class IV	17.5–49.9	High
Class V	50–100	Very high
Class VI	>100	Extremely high

IgE, immunoglobulin E.

For quantitative variables, mean, SD, and range (minimum and maximum) were computed. Independent *t*-test was used for quantitative normally distributed data for detecting the difference between two different groups. The χ^2 and Fisher's exact tests were used to detect the relation between different qualitative variables. Correlation estimates the amount of dependency of one factor on the other; the closeness of the association was measured by the correlation coefficient (*r*). The value of *r* ranges from +1 to −1. A test of significance (*t*-test for correlation) was used to test the level of significance of the association (to measure the *P*-value).

Validity included the following: sensitivity, which was defined as the proportion of participants with the disease who have a positive test for the disease; specificity, which was defined by the proportion of participants without the disease who have a negative test for the disease; positive predictive value, which was defined as the probability of disease in patients with a positive test result; negative predictive value, which was defined as the probability of not having the disease when the test result was negative; and accuracy, which is the proportion of all test results, whether positive or negative, which were correct.

Results

One hundred and twenty patients with allergic conjunctivitis were enrolled in this study. The male-to-female ratio in general was 1.26 (56% male and 44% female) and the mean age was 21.3 years (range: 7–48 years). The exception for this was VKC in which there was a significant male dominance (73%) and younger age with a mean of 11.5 years. Forty-five percent of all cases were students and 70% were from rural areas. The majority (40%) of the patients had PAC, 29% had SAC, 25% had VKC, and 6% had AKC.

Sixty percent of the patients had a positive family history of allergy, of whom 37% had allergic rhinitis, 30% had allergic conjunctivitis, 24% had bronchial asthma, and 9% had atopic dermatitis (Table 3).

There was a statistically significant difference in age and sex distribution in the VKC group with respect to the other groups.

Some allergic diseases can be associated with allergic conjunctivitis (Table 4).

In this study, the SPT and specific IgE were performed to 11 different allergens and the results revealed that the most common allergens were mixed pollen, mixed mould, and mixed mite (Fig. 2).

There was a statistically significant difference in grading results of the SPT, in which few cases were of grade 1 and no cases exceeded grade 4. No cases were positive to mixed mould in the AKC group, neither for the SPT nor for the IgE specific test (Table 5).

Table 3 Comparison between different studied groups in relation to age, sex, and family history

Data	PAC (*n*=48) [*N* (%)]	SAC (*n*=35) [*N* (%)]	VKC (*n*=30) [*N* (%)]	AKC (*n*=7) [*N* (%)]	*P* value
Sex					
Male	30 (62.5)	12 (34.3)	22 (73.3)	3 (42.9)	0.007[a]
Female	18 (37.5)	23 (65.71)	8 (26.7)	4 (57.1)	
Family history	29 (60.4)	16 (45.7)	23 (76.7)	4 (57.1)	0.08
Age (mean±SD) (years)	25.4±12.4	22.3±5	11.5±3	25.9±13.2	<0.001[a]

AKC, atopic keratoconjunctivitis; PAC, perennial allergic conjunctivitis; SAC, seasonal allergic conjunctivitis; VKC, vernal keratoconjunctivitis. [a]Fisher's exact test.

Table 4 Allergic diseases associated with allergic conjunctivitis

Associated diseases	PAC (*n*=48) [*N* (%)]	SAC (*n*=35) [*N* (%)]	VKC (*n*=30) [*N* (%)]	AKC (*n*=7) [*N* (%)]	*P* value
No accompanying disease	23 (47.9)	15 (42.9)	22 (73.3)	0 (0.0)	0.002[a]
Allergic rhinitis	16 (33.3)	13 (37.1)	6 (20.0)	0 (0.0)	0.140
Bronchial asthma	4 (8.3)	5 (14.3)	0 (0.0)	0 (0.0)	0.167
Eczema	0 (0.0)	0 (0.0)	0 (0.0)	6 (85.7)	<0.001[a]
Allergic rhinitis with asthma	1 (2.1)	0 (0.0)	1 (3.3)	0 (0.0)	0.764
Allergic rhinitis with Eczema	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0.116
Allergic rhinitis with Eczema and asthma	4 (8.3)	2 (5.7)	1 (3.3)	0 (0.0)	0.92

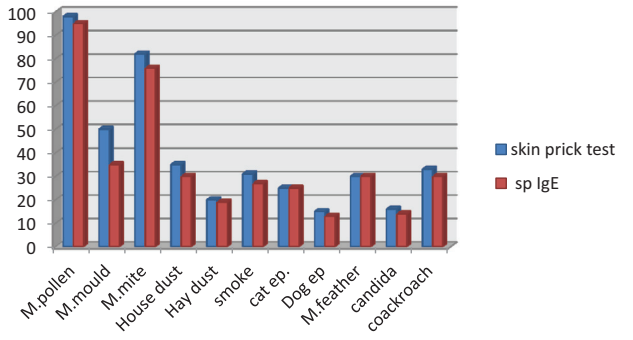
AKC, atopic keratoconjunctivitis; PAC, perennial allergic conjunctivitis; SAC, seasonal allergic conjunctivitis; VKC, vernal keratoconjunctivitis. [a]Test of significance is Fisher's exact test.

There was no statistically significant difference in IgE level to the most common allergens in the studied groups except for the SAC group. No cases were positive to mixed mould in the AKC group, neither for the SPT nor for the IgE-specific test (Table 6).

Validity of tear film-specific IgE in the detection of allergens inducing different types of allergic conjunctivitis was assessed against the SPT, which was used as a gold standard in this field (Tables 7–10).

There was IgE specificity of 100% and sensitivity ranging from 74 to 100% to the three conmen allergens in the PAC group (Table 7).

Figure 2



Bar chart showing the number of positive cases of the skin prick test and specific immunoglobulin E (IgE) to different allergens.

Table 5 Grading of skin prick test results to the most common allergens

Allergens	Grade 1 [*N* (%)]	Grade 2 [*N* (%)]	Grade 3 [*N* (%)]	Grade 4 [*N* (%)]	Grade 5 [*N* (%)]	*P* value
PAC						
Mixed pollen (*n*=35)	5 (14.3)	11 (31.4)	18 (51.4)	1 (2.9)	0 (0.0)	<0.001[a]
Mixed mite (*n*=40)	2 (5.0)	13 (32.5)	21 (52.5)	4 (10.0)	0 (0.0)	
Mixed mould (*n*=27)	0 (0.0)	13 (48.1)	13 (48.1)	1 (3.7)	0 (0.0)	
SAC						
Mixed pollen (*n*=31)	2 (6.5)	10 (32.2)	18 (58.1)	1 (3.2)	0 (0.0)	<0.001[a]
Mixed mite (*n*=15)	3 (20.0)	3 (20.0)	7 (46.7)	2 (13.3)	0 (0.0)	
Mixed mould (*n*=13)	2 (15.4)	4 (30.8)	5 (38.5)	2 (15.4)	0 (0.0)	
VKC						
Mixed pollen (*n*=25)	2 (8.0)	10 (40.0)	12 (48.0)	1 (4.0)	0 (0.0)	<0.001[a]
Mixed mite (*n*=23)	5 (21.7)	7 (30.4)	9 (39.1)	2 (8.7)	0 (0.0)	
Mixed mould (*n*=10)	3 (30.0)	1 (10.0)	5 (50.0)	1 (10.0)	0 (0.0)	
AKC						
Mixed pollen (*n*=7)	0 (0.0)	1 (14.3)	5 (71.4)	1 (14.3)	0 (0.0)	<0.001[a]
Mixed mite (*n*=4)	0 (0.0)	1 (25.0)	3 (75.0)	0 (0.0)	0 (0.0)	
Mixed mould	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	

AKC, atopic keratoconjunctivitis; PAC, perennial allergic conjunctivitis; SAC, seasonal allergic conjunctivitis; VKC, vernal keratoconjunctivitis. [a]Test of significance is Fisher's exact test.

Table 6 Classes of specific immunoglobulin E level to the most common allergens

Allergens	Class I [*N* (%)]	Class II [*N* (%)]	Class III [*N* (%)]	Class IV [*N* (%)]	Class V [*N* (%)]	*P* value
PAC						
Mixed pollen (*n*=32)	0 (0.0)	10 (31.2)	16 (50.0)	5 (15.6)	1 (3.1)	0.577
Mixed mite (*n*=36)	0 (0.0)	12 (33.3)	20 (55.6)	3 (8.3)	1 (2.8)	
Mixed mould (*n*=20)	0 (0.0)	11 (55.0)	7 (35.0)	2 (10.0)	0 (0.0)	
SAC						
Mixed pollen (*n*=30)	1 (3.3)	6 (20.0)	16 (53.3)	7 (23.3)	0 (0.0)	0.04
Mixed mite (*n*=13)	0 (0.0)	1 (7.7)	7 (53.8)	3 (23.1)	2 (15.4)	
Mixed mould (*n*=10)	3 (30.0)	2 (20.0)	4 (40.0)	0 (0.0)	1 (10.0)	
VKC						
Mixed pollen (*n*=22)	2 (9.1)	9 (40.9)	10 (45.5)	1 (4.5)	0 (0.0)	0.193
Mixed mite (*n*=23)	1 (4.3)	4 (17.4)	10 (43.5)	7 (30.4)	1 (4.3)	
Mixed mould (*n*=5)	0 (0.0)	1 (20.0)	2 (40.0)	2 (40.0)	0 (0.0)	
AKC						
Mixed pollen (*n*=6)	–	1 (16.7)	4 (66.7)	1 (16.7)	0 (0.0)	1.000
Mixed mite (*n*=4)	–	1 (25.0)	3 (75.0)	0 (0.0)	0 (0.0)	
Mixed mould (*n*=0)	–	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	

AKC, atopic keratoconjunctivitis; PAC, perennial allergic conjunctivitis; SAC, seasonal allergic conjunctivitis; VKC, vernal keratoconjunctivitis.

There was IgE specificity of 100% and sensitivity ranging from 77 to 97% to the three conmen allergens in the SAC group (Table 8).

There was IgE specificity of 100% and sensitivity ranging from 50% to 100% to the 3 conmen allergens in the VKC group (Table 9).

There was IgE specificity of 100% to mite and sensitivity ranging from 86% for pollen to 100% for mite in the AKC group (Table 10).

Correlations between the specific IgE test and the SPT in the studied groups are shown in Tables 11–15 and demonstrated in Figs 3–6.

There was a statistically significant correlation between the specific IgE test and the SPT in patients with

Table 7 Validity of detection of specific-immunoglobulin E test in the diagnosis of patients with perennial allergic conjunctivitis

Allergen	Sensitivity	Specificity	PPV	NPV	Accuracy
Pollen	91.42	100.0	100.0	81.25	93.75
Mite	100.0	100.0	100.0	100.0	100.0
Mould	74.07	100.0	100.0	75.0	85.41

NPV, negative predictive value; PAC, perennial allergic conjunctivitis; PPV, positive predictive value.

Table 8 Validity of detection of specific immunoglobulin E test in the diagnosis of patients with seasonal allergic conjunctivitis

Allergen	Sensitivity	Specificity	PPV	NPV	Accuracy
Pollen	96.77	100.0	100.0	80.0	97.14
Mite	86.66	100.0	100.0	90.9	94.28
Mould	76.92	100.0	100.0	88.0	91.42

NPV, negative predictive value; PPV, positive predictive value; SAC, seasonal allergic conjunctivitis.

Table 9 Validity of detection of specific immunoglobulin E test in the diagnosis of patients with vernal keratoconjunctivitis

Allergens	Sensitivity	Specificity	PPV	NPV	Accuracy
Pollen	92.0	100.0	100.0	71.4	93.33
Mite	100.0	100.0	100.0	100.0	100.0
Mould	50.0	100.0	100.0	83.33	80.0

NPV, negative predictive value; PPV, positive predictive value; VKC, vernal keratoconjunctivitis.

Table 10 Validity of detection of specific immunoglobulin test in the diagnosis of patients with atopic keratoconjunctivitis

Allergen	Sensitivity	Specificity	PPV	NPV	Accuracy
Pollen	85.71	0.0	100.0	0.0	85.71
Mite	100.0	100.0	100.0	100.0	100.0
Mould	0.0	0.0	0.0	0.0	0.0

AKC, atopic keratoconjunctivitis; NPV, negative predictive value; PPV, positive predictive value.

Table 11 Correlation between the specific immunoglobulin E test and the skin prick test in patients with perennial allergic conjunctivitis

	Specific IgE	
Variable	*r*	*P* value
Skin prick test		
Pollen	0.851	<0.001
Mite	0.826	<0.001
Mould	0.861	<0.001

IgE, immunoglobulin E.

Table 12 Correlation between the specific immunoglobulin E test and the skin prick test in patients with seasonal allergic conjunctivitis

	Specific IgE	
Variable	*r*	*P* value
Skin prick test		
Pollen	0.821	<0.001
Mite	0.964	<0.001
Mould	0.811	0.02

IgE, immunoglobulin E; SAC, seasonal allergic conjunctivitis.

Table 13 Correlation between the specific immunoglobulin E test and the skin prick test in patient with vernal keratoconjunctivitis

	Specific IgE	
Variable	*r*	*P* value
Skin prick test		
Pollen	0.802	<0.001
Mite	0.894	<0.001
Mould	0.861	0.061

IgE, immunoglobulin E.

Table 14 Correlation between the specific immunoglobulin E test and the skin prick test in patients with atopic keratoconjunctivitis

	Specific IgE	
Variable	*r*	*P* value
Skin prick test		
Pollen	0.826	0.043
Mite	1.000	<0.001
Mould	–	–

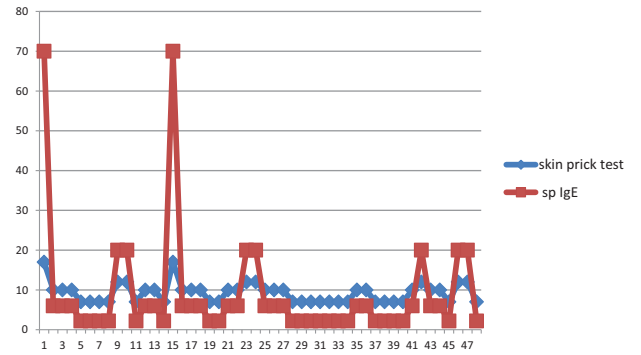
IgE, immunoglobulin E.

Table 15 Correlation between the specific immunoglobulin E test and the skin prick test in all studied groups

	Specific IgE	
Variable	*r*	*P* value
Skin prick test		
PAC	0.871	<0.001
SAC	0.839	<0.001
VKC	0.790	<0.001
AKC	0.829	0.02

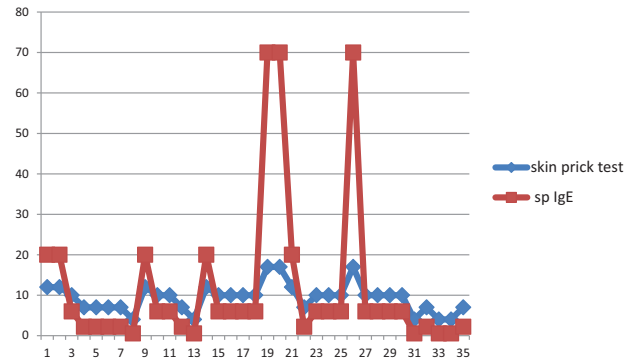
AKC, atopic keratoconjunctivitis; PAC, perennial allergic conjunctivitis; SAC, seasonal allergic conjunctivitis; VKC, vernal keratoconjunctivitis.

Figure 3



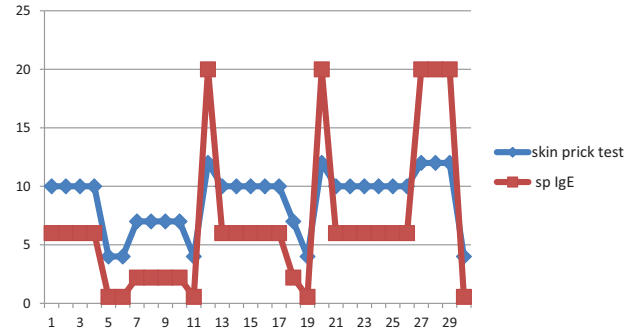
Correlation between the specific immunoglobulin E (IgE) test and the skin prick test in patients with perennial allergic conjunctivitis.

Figure 4



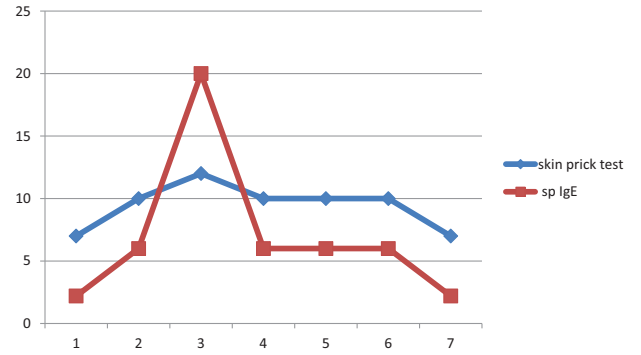
Correlation between the specific immunoglobulin E (IgE) test and the skin prick test in patients with seasonal allergic conjunctivitis.

Figure 5



Correlation between the specific immunoglobulin E (IgE) test and the skin prick test in patients with vernal keratoconjunctivitis.

Figure 6



Correlation between the specific immunoglobulin E (IgE) test and the skin prick test in patients with atopic keratoconjunctivitis.

Perennial allergic conjunctivitis (PAC) (Table 11 and Fig. 3).

There was a statistically significant correlation between the specific IgE test and the SPT in patients with SAC (Table 12 and Fig. 4).

There was a statistically significant correlation between the specific IgE test and the SPT in patients with VKC except for mould allergen (Table 13 and Fig. 5).

There was only a statistically significant correlation between the specific IgE test and the SPT for mite allergen in patients with AKC (Table 14 and Fig. 6).

There was a statistically significant correlation between the specific IgE test and the SPT in all studied groups (Table 15).

Discussion

Allergic diseases have dramatically increased in the last decades [19]. Ocular allergy represents one of the most common ocular conditions encountered in clinical practice [20].

Allergic conjunctivitis diseases are among the main ocular surface disorders primarily caused by type I allergic reaction. Allergic conjunctivitis diseases are classified into four clinical forms: SAC, PAC, VKC, and AKC [20].

PAC and SAC are the most common types of ocular allergies and are said to affect at least 15–20% of the population [20]. In the present study, the majority (40%) of the patients had PAC, 29% had SAC, 25% had VKC, and 6% had AKC.

In this study, the most common accompanying allergic disease was allergic rhinitis followed by bronchial asthma and eczema, although eczema was the most common accompanying allergic disease among patients with AKC. This is in accordance with Kocatürk *et al.* [16], who found that 73.7% of their patients had allergic rhinitis. Higher percentages of associated allergic rhinitis were found by Hesselmar *et al.*

(88%) [21] and Kosrirukvongs *et al.* (92%) [22]. As patients with allergic conjunctivitis often present with varying symptoms of rhinitis, many studies usually use unspecific terms such as hay fever or allergic rhinoconjunctivitis for such allergies [23].

Approximately half of the patients had a family history of other allergic conditions such as allergic rhinitis, atopic dermatitis, and asthma [16]. In the present study, 60% of the patients had a positive family history of allergy. This may indicate the role of the genetic factors in the development of allergic rhinoconjunctivitis [24].

The diagnosis of ocular allergy is primarily clinical, but there are laboratory tests that can be useful in supporting the diagnosis. Allergists can perform skin testing for specific allergens using SPT or intradermal injections of allergen [20].

Skin testing represents the primary diagnostic tool in allergy and is considered the gold standard in this field. It is used to confirm that a specific allergen has induced an IgE antibody response [25].

In-vitro tests for IgE antibodies to specific allergens are widely used [20]. IgE has been considered to play an important role in allergic reactions in the eye; thus, they can be used in diagnosing allergic conjunctivitis [26].

This study was conducted to measure tear IgE concentrations in different types of allergic conjunctivitis and to detect the sensitivity and specificity of this test in relation to the SPT (gold standard).

Usually, diagnosis of allergic diseases is performed by measuring serum IgE concentration. However, this does not differentiate between local and systemic allergy [18].

Inflammatory cells have a very essential function in regulating IgE production at local levels in reactions such as allergic conjunctivitis. Locally formed IgE combines with the antigen and attaches to the surface of local mast cells. Subsequently, these cells move into the systemic circulation, and, although local concentrations of IgE may be high, systemic concentrations will be extremely low [27].

Friedlaender *et al.* [28] found that measurement of IgE in tear samples is not only useful for the diagnosis of allergic conjunctivitis but also for the assessment of the severity of the allergy.

In the present study, there were strong correlations between the level of specific IgE using Immune blot assay for the tear samples and the results of the SPT (r=0.871, 0.839, 0.790, and 0.829) in the studied groups, respectively, with a P-value less than 0.05 in all studied groups. This is in accordance with Wohrl *et al.* [29], who found that the agreement between the in-vitro-specific IgE antibody assays and SPT results was between 85 and 95%. In addition, Demir *et al.* [30] found that, except for mould, all allergens had significant correlations between their specific IgE levels and skin test positivity. Cho *et al.* [31] stated that there was 81–97% agreement between SPT and individual specific IgE test in allergen detection.

The sensitivity and specificity of immunoassays for IgE differ with the system being used and the quality of the allergen. Overall IgE sensitivity ranges from 60 to 95% and specificity from 30 to 95% [32,33]. In the current study, there was a high sensitivity to pollen (91.42, 96.77, 92, and 85.71%) and mite (100, 86.66, 100, and 100%) in the four groups, respectively, a high sensitivity to mould (74.07, 76.92, and 50%) in the first three groups, respectively, (no allergy to mould was seen in the AKC group), and a high specificity to pollen (100, 100, 100, and 100%) and mite (100, 100, 100, and 100%) in the four groups, respectively, and to mould (100, 100, and 100%) in the first three groups, respectively, (no allergy to mould was seen in the AKC group). This is in accordance with the results of Attia *et al.* [34], who found that the statistical evaluation results as regards commercial specific IgE sensitivity, specificity, positive predictive value, and negative predictive value were 93.1, 88.9, 96.2, and 93.7%, respectively. Williams *et al.* [35] recorded values of more than 90% sensitivity and 100% specificity for specific IgE of pollens of common grasses and trees, dust mites, and cat allergens.

In contrast to the current study results, Popiel *et al.* [36] found that the sensitivity of the group of home dust mites was 85% and specificity was only 40%, and, in case of the group of storage mites, the sensitivity was on the level of as much as 90.24% and the specificity, however, was only on the level of 25%. The sensitivity is quite high. Unfortunately, the specificity of these tests is deficient in their study.

Skin tests are the most clinically appropriate techniques in the evaluation of allergic patients by determinations of IgE-mediated hypersensitivity because of their ease, natural relevance in the patient's own skin, low cost, high sensitivity, and little time of performance [37]. Skin tests as with other physiologic procedures

necessitate a degree of expertise by the observer to both interpret the results and link them with the history and physical findings. As with other diagnostic studies, inappropriately performed or interpreted skin test can lead to false-positive or false-negative results. However, cutaneous responsiveness varies between patients, and hence positive result will be clearer in some patients than others. Thus, other factors may play a role in correct interpretation, such as patient's history and the patient's response to antigens and controls [25].

There are many other limitations to skin testing. For example, skin testing should generally be performed on normal skin and the test should be performed with a physician available to treat side effects, including anaphylaxis [38].

Antihistamines, tricyclic antidepressant [38], and some tranquilizers suppress the wheal and flare response and should be discontinued before allergy testing for up to 10–19 days or even more [39]. Skin testing in patients taking beta blocking agents has a risk of an exaggerated adverse reaction [40].

Skin test sensitivity may be altered by long-term corticosteroid treatment but short-time treatment does not have the same effect. As regards pregnancy, SPT is safe, but if adverse reaction occurs, such as anaphylaxis, the fetus might be adversely affected [41].

Skin test reactions can vary with age, with infants and older adults having less reactivity. In addition, patients need to be old enough to be able to cooperate with testing [25]. Skin test reactions may be more difficult to interpret in patients with dark skin or any cutaneous lesion that may interfere with the skin test reactivity [25]. Some patients with chronic diseases such as diabetes, renal failure, cancer, and spinal cord injuries may have a decrease in skin sensitivity [42].

All of the above-mentioned limitations to skin test should redirect the allergists' and ophthalmologists' attention to the other more simple and convenient tests such as specific IgE testing in the tear film, especially if it is easy and have a good correlation and validity in relation to skin testing.

Conclusion

Tear film-specific IgE has a statistically significant correlation and validity when compared with the SPT in diagnosing the causative allergen in different types of allergic conjunctivitis. Tear IgE concentrations can be measured in small tear samples easily and less frightening, especially to a young patient and not affected by patients age, skin lesions, skin color, and chronic diseases. Therefore, tear-specific IgE could be a good alternative to SPT in the diagnosis of allergic conjunctivitis with high sensitivity and specificity and fewer complications and limitations.

Acknowledgements

Basem M. Ibrahim contributed to the design, definition of intellectual content, literature search, clinical studies, data acquisition, data analysis, manuscript preparation, manuscript editing, and manuscript review. Randa S. Abdel-Latif contributed to the concept, design, literature search, experimental studies, data acquisition, data analysis, statistical analysis, and manuscript review.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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