



One-year evaluation of clinical and immunological efficacy and safety of sublingual versus subcutaneous allergen immunotherapy in allergic conjunctivitis

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Abstract

Background The aim of this study is to evaluate the clinical and immunological efficacy and safety of allergen immunotherapy (AIT) in patients with allergic conjunctivitis (AC) and to compare between sublingual and subcutaneous routes of administration.

Methods A prospective comparative case series study was performed on 100 patients with IgE-mediated AC. Patients were referred to allergy clinics for skin prick test (SPT) and AIT. Patients with positive SPT and high-serum IgE level were enrolled in this study. Patients were divided into two groups: sublingual immunotherapy (SLIT) group (50 patients) and subcutaneous immunotherapy (SCIT) group (50 patients). Both groups were followed for 1 year. Efficacy was assessed clinically by comparing pre- and post-treatment symptoms and medication scores and assessed immunologically by comparing pre- and post-treatment serum IgE level and wheal diameter of SPT. Safety of the therapy was assessed by the occurrence of adverse reactions and patient tolerability to the therapy.

Results Patients were either mono- or polysensitized to different allergens. Aeroallergens were significantly more common than food allergens ($P = 0.00$). The most prevalent aeroallergens were pollens (40%) and house dust (30%). At 12-month follow-up, both routes SLIT and SCIT led to a statistically significant clinical and immunological improvement ($P < 0.05$). This improvement was evident in all follow-up parameters including total ocular symptom score (TOSS), medication score, total serum IgE level, and wheal diameter of skin prick test (SPT). There was no significant difference between the two routes of administration (SLIT & SCIT) in any of the follow-up parameters ($P > 0.05$). Patients were able to tolerate the allergen therapy without developing any serious adverse events.

Conclusion Aeroallergen polysensitization is common among patients with AC. SPT should be included in the diagnostic workup of those patients. AIT is a safe and effective treatment option for patients with AC as it has the potential to achieve significant reduction in symptom and medication scores without ocular or systemic side effects. There is no significant difference between both routes of administration either SLIT or SCIT in achieving clinical and immunologic improvement; so the patient can choose his preferred method for therapy.

Keywords Allergic conjunctivitis · Skin prick test · Subcutaneous immunotherapy · Sublingual immunotherapy

Introduction

Allergic conjunctivitis is a hypersensitivity reaction affecting the ocular surface being predominantly an IgE-mediated

hypersensitivity immunological reaction to environmental allergens [1]. Allergic conjunctivitis is further subclassified into perennial AC, seasonal AC, and the more severe forms of AC, including vernal keratoconjunctivitis (VKC) and atopic keratoconjunctivitis (AKC).

The term AC is an inclusive term that involves different clinical types based on the assumption that the classical type I hypersensitivity mechanism is responsible for all clinical forms of allergic eye disease. However, IgE- and non-IgE-mediated mechanisms are included in the development of ocular allergy [2]. The diagnosis of AC is mainly clinical and depends on a case history. Treatment options include various topical agents as mast cell stabilizers, antihistamines, and

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topical steroids. Frequent long-term use of local steroids may lead to many complications such as glaucoma and cataract [3]. It would therefore appear necessary to attempt an alternative therapy in cases where frequent steroid use is becoming a matter of concern.

Evaluation by SPT is usually overlooked in patients with AC [4]. It is a reliable method to diagnose IgE-mediated allergy and identifying the causative allergens [5]. Specific allergen immunotherapy (SIT) with increasing doses of the causative allergen is the only treatment modality with the capacity of changing the natural course of allergy [6] and could induce clinical and immunologic tolerance [7] by pushing the body to develop a normal immune response to the allergen, rather than the intense reaction that it develops with exposure to this allergen, which includes burning sensation, redness, severe itching, and watery eyes [8].

Allergen immunotherapy has been indicated as a treatment option for several allergic conditions including allergic rhinitis or allergic asthma [9]. Immunotherapy for allergic rhinitis (AR) has been shown to have disease-modifying effects and result in long-term remission of allergic symptoms with reduction of the risk of progression from rhinitis to asthma, as well as the chances of developing new sensitizations to allergens [7].

Regarding AIT in AC, studies are very limited and unsatisfactory either due to studying one type of ocular allergy, evaluation of one type of allergen, insufficient follow-up parameters, or small sample size.

To the best of our knowledge, no previous studies have evaluated both the clinical and immunological efficacy and safety of AIT in patients with IgE-mediated AC using multiple allergen preparations therapy in a prospective design, nor compared the 2 main routes of administration SLIT vs. SCIT.

The aim of this study is to try to overcome the limitations of the previous studies, evaluate the efficacy and safety of AIT in AC, and to compare between SLIT and SCIT.

Main outcomes are (1) clinical improvement in the form of improvement of total ocular symptoms score (TOSS) and medication score, (2) immunological improvement in the form of regression of skin reactivity in SPT and reduction of total serum IgE level, and (3) safety assessment in the form of occurrence of adverse reactions.

Patients and methods

Study design

The study is a prospective comparative case series study. It was conducted in both Ophthalmology department and Allergy unit in Respiratory medicine department, Sohag University from October 2017 and October 2018. The study was approved by the Local Ethical Committee of

Sohag University and was conducted in accordance with the Declaration of Helsinki.

Patient selection

Patients diagnosed with AC who are resistant to steroid sparing agents or those who are unsatisfied with using eye drops for long time were referred to Allergy unit in Respiratory medicine department, Sohag University for SPT and estimation of total serum IgE level to confirm type 1 hypersensitivity then AI was started after written informed consent.

Exclusion criteria

Patients younger than 6 years old and patients with other possible causes of elevated serum IgE level as parasitic infestations were screened and excluded. Patients with history of anaphylaxis have negative SPT or low IgE level. Patients who did not complete 1-year follow-up were also excluded.

The study was conducted on 100 patients (who met the inclusion criteria). Patients were divided into two groups: SLIT group included 50 patients treated by SLIT and SCIT group included 50 patients treated by SCIT. Both groups were followed for 1 year. Efficacy was assessed clinically by comparing pre- and post-treatment symptom and medication scores, and assessed immunologically by comparing pre- and post-treatment wheal diameter of skin prick test and total serum IgE level. Safety of the therapy was assessed by the occurrence of adverse reactions and patient tolerability.

Skin prick testing

The panel for skin testing was composed of 30 different common allergen extracts for both inhaled and ingested allergens (Table 2) together with histamine and saline as positive and negative controls respectively. A drop of solution of each allergen was placed on the flexor surface of the forearm, and a midpoint was used to prick the skin. A drop of saline 0.9% and a drop of histamine phosphate were used as a negative control and positive control respectively. A lancet (Dome-Hollister-Stier) was used to prick the skin at a 90° angle through a drop of test solution on the skin [10]. SPT was evaluated at 20 min. A wheal diameter ≥ 3 mm more than the negative control was considered to be positive [11]. Reaction to 30 allergens was tested before start and after 1 year of the course of the SIT. Patients had to stop steroids and antihistamines 48 h before the test.

Serum total IgE level

Enzyme-linked immunosorbent assay (ELISA) was used for the quantitative determination of IgE concentration in human

serum. The total IgE level in a normal, allergy-free adult is less than 100 IU/ml of serum.

Allergen preparation and treatment schedule

Extracts were prepared as glycerinated solution, using the wt/vol method [12]. Patients were prescribed oral antihistamines 2 h before each dose to reduce the frequency of any systemic reactions [13]. The dosing regimens and allergen equivalence for the SCIT and SLIT groups were as previously reported [14].

Briefly, SLIT was self-administered at home and taken on an empty stomach as sublingual drops kept under the tongue for 2 min then swallowed. Patients were prohibited to drink or eat any foods for 5 min after swallowing the drops. SCIT was administered in the clinic and the patients were observed for at least 30 min after each injection for possible adverse effects.

Post-treatment follow-up parameters

Assessment of clinical efficacy

Total ocular symptom score The Total Ocular Symptom Score (TOSS) is a questionnaire used by allergists to assess eye symptoms in patients with allergic conjunctivitis [15]. It assesses the frequency of symptoms commonly associated with allergic conjunctivitis: itching, redness, tearing, and swelling by the following steps:

1. Add up scores for each symptom

All of the time = 4, most of the time = 3, half of the time = 2, some of the time = 1, none of the time = 0

2. Divide by maximum score

All 4 questions (one question for each symptom answered divide by 16, 3 questions answered divide by 12, 2 questions answered divide by 8, 1 question answered divide by 4)

3. Multiply by 100

Score example:

Itchy = 4, red = 3, tearing = N/A, swelling = 2, total: 9
“3 questions answered divide by 12”

$9/12 \times 100 = 75.0$

Medication score Medication usage was scored on a 4-point scale. Scores are assigned to the different medications as follows: 0 = no medication taken; 1 = patient took antihistamines; 2 = patient took topical corticosteroids; and 3 = patient took oral corticosteroids. Patients were

considered improved if the total score decreased by one or more points [16].

Assessment of immunological efficacy

Immunological efficacy is assessed by changes in wheal diameter of skin reactivity and in total IgE antibody levels before and after treatment.

Safety assessment The safety analysis was based on the reported symptoms and adverse events by patients and doctors and their global assessment of tolerability at the end of the study.

Statistical analysis

All statistical analyses were performed using SPSS ver. 20 (SPSS Inc., Chicago, IL, USA). The values are presented as mean $\pm$ standard deviation. Student's *t* test was used to analyze differences between the 2 groups. Paired *t* test was used to compare pre- and post-treatment means. Z test was used to compare between 2 proportions. Pearson or Spearman method was used to test correlation. The level of significance was ($P < 0.05$).

Results

Clinical characteristics

One hundred patients with IgE-mediated AC were enrolled in this study. Only 93 patients have completed their estimated follow-up period (12 ms). Allergic conjunctivitis was diagnosed by symptoms and signs of ocular allergy and proven by skin prick test and a serum IgE level. Mean age of the study population was 23.35 ± 13.06 (range 6–55 years). Baseline mean TOSS and medication score were 87.545 ± 12.55 and 2.27 ± 0.44 respectively. Baseline mean serum total IgE level and wheal diameter of skin prick test were 387.99 ± 389.65 and $8.64 \text{ mm} \pm 3.02$ respectively.

There was no statistically significant difference between SLIT and SCIT groups in either age (22.8 ± 15.16 vs. 23.9 ± 10.70 ; $P = 0.67$) or sex (26/24 vs. 22/28; $P = 0.42$) (Table 1).

There was no significant difference between both groups in either baseline mean TOSS (87.99 ± 13.27 vs. 87.1 ± 11.89 ; $P = 0.72$), medication score ($2.340 \pm .47$ vs. $2.2 \pm .40$; $P = 0.11$), serum IgE level (403.96 ± 421.54 vs. 372.02 ± 358.52 ; $P = 0.68$), or mean wheal diameter of skin prick test (8.94 ± 3.13 vs. 8.34 ± 2.9 ; $P = 0.32$) for SLIT and SCIT groups respectively (Table 1, Figs. 1 and 2).

Table 1 Demographics and baseline characteristics of the 2 study groups

Characteristic	SLIT group (n = 50)	SCIT group (n = 50)	P value
Age (year)	22.8 ± 15.16	23.9 ± 10.70	0.67
Sex (male/female)	26/24	22/28	0.42
TOSS	87.99 ± 13.27	87.1 ± 11.89	0.72
Medication score	2.340 ± 0.47	2.2 ± 0.40	0.11
Total IgE (mean, kU/L)	403.96 ± 421.55	372.02 ± 358.52	0.68
Mean wheal diameter (mm) of SPT	8.94 ± 3.13	8.34 ± 2.91	0.32
Type of sensitization			
Monosensitization	8%	12%	0.51
Polysensitization	92%	88%	0.51

SLIT sublingual immunotherapy, SCIT subcutaneous immunotherapy, SPT skin prick test, TOSS total ocular symptoms score

Prevalence of the commonest allergens in patients with allergic conjunctivitis

The most common aeroallergens were “Pollens” 40%, followed by “House Dust” 30%, “House Dust Mite” 28%, “Hay dust (HD)” 24%, followed by cockroach, feather, and mixed molds. Food allergy was positive only in 10%. The most prevalent food allergens were cow’s milk, fish, eggs, and wheat flour (Table 2). Among different age groups, the most common allergens were (pollens, house dust, feather, and cockroach) for patients aged 6–12 years and (pollens, mites, house dust, and hay dust) for patients > 12 years.

Regarding type of sensitization of SPT, in SLIT group, 4 patients (8%) were monosensitized (2 patients were sensitive for pollens, 1 for house dust mites, 1 for pigeon feather) and 46 patients (92%) were polysensitized. For SCIT group, 6 patients (12%) were monosensitized (4 patients for pollens, 1 for hay dust, 1 for house dust mites) and 44 (88%) patients were polysensitized (Table 1).

Post-immunotherapy follow-up parameters: (Figs. 1 and 2)

Clinical parameters: TOSS and medication score

Seven patients did not complete their follow-up period of 12 months (4 patients of SCIT group and 3 patients of SCIT group).

For the whole study population (93 patients), mean post-IT TOSS was 20.41 ± 15.73 , mean medication score was 0.26 ± 0.56 . A significant reduction of TOSS and medication score were observed in all patients 1 year following immunotherapy when compared to baseline $P = 0.00$ (Table 3).

For SLIT group, mean post-treatment TOSS and mean medication score were 22.64 ± 20.58 and 0.34 ± 0.62 respectively. A significant reduction of both scores were observed following SL immunotherapy when compared to baseline $P = 0.00$ (Table 4).

Similarly, in SCIT group, mean post-treatment TOSS and mean medication score were 18.17 ± 8.11 and $0.18 \pm .48$

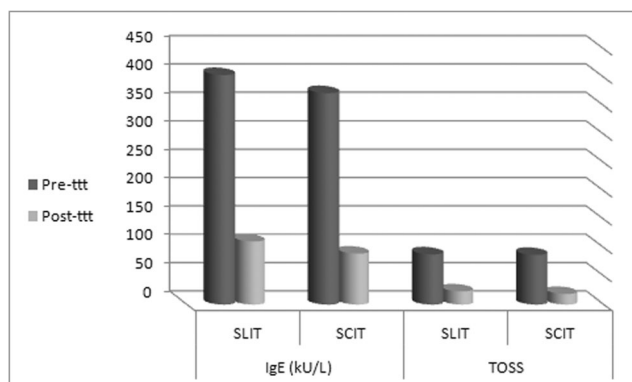


Fig. 1 IgE level and TOSS before and after immunotherapy in both groups. SLIT, sublingual immunotherapy; SCIT, subcutaneous immunotherapy; TOSS, total ocular symptoms score; ttt, treatment

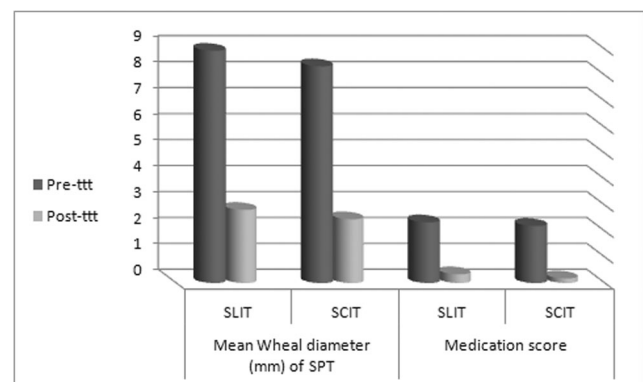


Fig. 2 Medication score and mean wheal diameter of SPT before and after immunotherapy in both groups. SLIT, sublingual immunotherapy; SCIT, subcutaneous immunotherapy; SPT, skin prick test; ttt, treatment

Table 2 Prevalence of allergen sensitivity in the whole study population

	Prevalence%
Aeroallergens	
Mixed pollens	40
House dust	30
Mites	28
Hay dust	24
Cockroach	18
Feather	18
Mixed molds	18
Aspergillus fumigates	8
Pigeon	8
Tobacco	8
Straw	6
Wool	4
<i>Candida albicans</i>	4
Cotton dust	4
Latex	4
Aspirin	3
Cat hair	2
Dog hair	2
Horse hair	1
Honey bee venom	1
Food allergens	
Milk	4
Fish	3
Egg	3
Wheat flour	2
Cocoa	1
Peanut	1
Soya bean	1
Strawberry	1
Solanaceae	1
Banana	1

respectively. A significant reduction of both scores were observed following SC immunotherapy when compared to baseline $P = 0.00$ (Table 4)

There was no significant difference between both groups in the post-immunotherapy TOSS (26.22 ± 21.28 vs. 22.58 ± 21.47 ; $P = 0.58$) or medication score (0.57 ± 0.59 vs. 0.59 ± 0.59 ; $P = 0.885$) for SLIT and SCIT groups respectively.

Table 3 Comparison of the follow-up parameters in the whole study population before and after immunotherapy

	Pre-ttt	Post-ttt	<i>P</i> value
TOSS	87.545 ± 12.55	20.41 ± 15.73	0.00
Medication score	2.27 ± 0.44	$0.26 \pm .56$	0.00
IgE (kU/L)	387.99 ± 389.65	100.12 ± 74.71	0.00
Mean wheal diameter (mm) of SPT	8.64 ± 3.02	2.64 ± 1.23	0.00

SPT skin prick test, TOSS total ocular symptoms score, ttt treatment

Immunological parameters (mean IgE and mean wheal diameter of SPT)

With respect to total IgE, all patients had a high baseline total IgE level (> 100 IU/ml). It ranged from 102 to 2200 IU/ml with mean of 387.99 ± 389.65 IU/ml.

For the whole study population; mean post-IT IgE level and wheal diameter of SPT were 100.12 ± 74.71 and 2.64 ± 1.23 respectively. A significant reduction of total serum IgE level and wheal diameter of SPT were observed in all patients following immunotherapy when compared to baseline $P = 0.00$ (Table 3).

For SLIT group, mean post-treatment IgE level and wheal diameter of SPT were 110.78 ± 80.28 and 2.82 ± 1.28 respectively. A significant reduction was observed following SL immunotherapy when compared to baseline $P = 0.00$ (Table 4).

Similarly, in SCIT group mean post-treatment IgE level and wheal diameter of SPT were 89.46 ± 67.82 and 2.46 ± 1.16 respectively. A significant reduction was observed following SL immunotherapy when compared to baseline $P = 0.00$ (Table 4).

There was no significant difference between both groups in either post-immunotherapy IgE (110.78 ± 80.28 vs. 89.46 ± 67.82 ; $P = 0.15$) or wheal diameter of SPT (2.82 ± 1.28 vs. 2.46 ± 1.16 ; $P = 0.14$) for SLIT and SCIT groups respectively.

There were no detectable new sensitizations with SPT 1 year after immunotherapy in either group (Table 5).

Safety assessment

Treatment with Specific Allergen IT was well tolerated in both study groups along the 1-year follow up. The most frequent adverse reactions were local redness and edema at the injection site (SLIT), oral pruritus (in SLIT), and fatigue. These occurred during the build-up phase which required dose reduction but did not require discontinuation. Most of the reactions were mild, completely recovered within few weeks without any reported complications. No systemic or severe adverse reaction was reported. The results of safety assessment are summarized in Table 6.

Clinical improvement (1-year success) was 93.6% achieved in all but 6 patients ($6/93 = 6.4\%$).

Table 4 Comparison of the follow-up parameters before and after immunotherapy in both groups

		Pre-ttt	Post-ttt	<i>P</i> value
TOSS	SLIT	87.99 ± 13.27	22.64 ± 20.58	0.00
	SCIT	87.1 ± 11.89	18.17 ± 8.11	0.00
Medication score	SLIT	2.340 ± .47	0.34 ± 0.62	0.00
	SCIT	2.2 ± .40	0.18 ± 0.48	0.00
IgE (kU/L)	SLIT	403.96 ± 421.55	110.78 ± 80.28	0.00
	SCIT	372.02 ± 358.52	89.46 ± 67.82	0.00
Mean wheal diameter (mm) of SPT	SLIT	8.94 ± 3.13	2.82 ± 1.28	0.00
	SCIT	8.34 ± 2.91	2.46 ± 1.16	0.00

SLIT sublingual immunotherapy, *SCIT* subcutaneous immunotherapy, *SPT* skin prick test, *TOSS* total ocular symptoms score, *ttt* treatment

Discussion

Characterization of allergens in patients with AC in each area is necessary and has an important role in the diagnosis and management of allergic disorders with possibility of performing immunotherapy. SPT is an important tool in identifying allergens that can cause allergic diseases. Our study was designed to highlight aeroallergen and food sensitization in patients with IgE-mediated AC, to evaluate the clinical and immunological efficacy and safety of allergen immunotherapy and also to compare between sublingual and subcutaneous routes of administration. Allergens tested in the study were selected according to our geographic features.

In the study, mixed pollens were the highest percentage of aeroallergen sensitization (40%) followed by house dust (30%), mites (28%), and hay dust (24%). These results are in agreement with a Greece study which demonstrated higher values of sensitization to pollen and household dust, but lower to animals [17]. The results were also in agreement with Navarro et al. study in Spain in which of 65% allergic rhinitis (AR) patients who had also conjunctivitis, pollen was the most frequent allergen (51%) followed by dust mites (42%) [18]. A recent Egyptian study showed that 65% of patients with VKC were sensitive to pollens and 55% to house dust [8]. By comparing these results, we can conclude that pollens and house dust are the aeroallergens that have the upper hand in triggering ocular allergy regardless the geographic area.

Table 5 Comparison of post-immunotherapy follow-up parameters in both groups

	SLIT	SCIT	<i>P</i> value
Post-IgE	110.78 ± 80.28	89.46 ± 67.82	0.15
Post-TOSS	22.64 ± 20.58	18.17 ± 8.11	0.15
Post-medication score	.34 ± .62	.18 ± .48	0.15
Post-wheal diameter of SPT	2.82 ± 1.28	2.46 ± 1.16	0.14

SLIT sublingual immunotherapy, *SCIT* subcutaneous immunotherapy, *SPT* skin prick test, *TOSS* total ocular symptoms score, *ttt* treatment

On the other hand, the role of food allergens in triggering AC has not been studied before. Our study revealed positive food allergy in only 10% of the study population that suggests a minimal role that food allergens represent in contrast to the most common areoallergens. The most prevalent food allergens were cow's milk, fish, eggs, and wheat flour. Cases of AR triggered by food were also reported to be uncommon [19]. Allergic conjunctivitis and AR have a close epidemiologic relationship. Both conditions also exhibit similar pathophysiologic mechanisms [20].

Most of our study population (90%) were polysensitized to two or more allergens, only 10% were monosensitized. Type of sensitization either mono- or polysensitization in AC has not been studied before. Polysensitization was reported to be common in patients with AR. However, there are patients who remain monosensitized [21]. Factors that lead to multi-allergen sensitization include environmental factors, genetics, and cross-sensitization between botanically closed species sharing common allergenic epitopes [22]. Ciprandi et al. estimated that percentage of polysensitized patients may widely range from 20 to 90% [23]. Fasce cited that polysensitization was a secondary phenomenon that always followed monosensitization [24]. Our study reported that polysensitization is significantly much more common in AC than monosensitization.

The study included patients with IgE-mediated AC only, this was due to a number of reasons: first AC is predominantly

Table 6 Safety assessment (treatment-emergent adverse events reported)

Adverse events	(%)
Local irritation	48
Oral pruritus	12
Ear pruritus	10
Throat irritation	5
Eye pruritus	4
Skin pruritus	3
Chest tightness	3
Headache	3
Fatigue	1

type 1 hypersensitivity although non-IgE mechanism is also involved, the second is allergen IT is based on detection of the causative allergen and desensitization, the third reason is to obtain quantitative parameters for accurate follow up of immunological improvement in the form of serum IgE level and wheal diameter of skin prick test.

Several studies reported that the clinical and immunological efficacy of allergen IT reached a statistical significance after the first year of immunotherapy [14, 25]. Therefore, we followed our study population for 1 year. One-year follow-up is also sufficient for the patient to notice improvement of symptoms in the same season of the year in which exacerbation had previously occurred so the patient could feel the difference before and after IT especially for seasonal AC.

To our knowledge, no prospective studies have been done on the effect of AIT on patients with IgE-mediated AC nor have compared the clinical and immunological efficacy and safety between SLIT and SCIT. We compared efficacy of these two treatment modes on clinical and immunologic parameters. Previous studies reported significant improvement in both symptoms and sign scores with AIT for treating patients with AR and asthma [26–28]. Few studies have evaluated AIT in AC and they have either studied the identification of the causative allergens [29], one type of AC [8, 25], or AC caused by one type of allergen [25]. Our results reported a significant clinical and immunological improvement in patients with IgE-mediated AC following AIT. Clinical improvement was previously reported with Mahdy et al. [8] and Prakash et al. [30] with AIT for resistant VKC with success rate ranged from (50–62%). This is in contrast our high success rate of 93.6%; this discrepancy may be because we included all types of AC as long as it is IgE-mediated in contrast to other studies which included resistant VKC only.

There are some factors affecting patient response to IT as good patient education (patient non-compliance of allergen is reported to be the main reason for poor treatment response) [31]. Some patients may also discontinue their dosing regimen once they notice improvement of symptoms; avoidance of food intake immediately after sublingual drops (for SLIT) is mandatory for successful therapy and also avoidance of exposure to the causative allergen during the course of IT, for example, we started immunotherapy for patients with pollen-induced AC in pollen free season so air loaded with pollen does not interfere with the allergen-dosing regimen received by the patient.

The decision to use one route of administration or the other is sometimes made by the patient, sometimes advised by the treating physician. Economical considerations, living far from the office, busy schedule, or “needle phobia” are examples of when a patient may chose SLIT. Being a very young patient and having severe skin or medical problems that may render

administration of SCIT risky are examples of why the treating physician will advise SLIT [32]. The study reported no significant difference between both routes of administration of IT either sublingual or subcutaneous in inducing clinical or immunological improvement.

This is in agreement with previous studies [33, 34] comparing both routes of therapy. Diego Saporta [32] and Nelson [35] have studied both routes in managing patients with AR and asthma; they found no difference between them. Studies comparing routes of administration of immunotherapy in AC are limited. Ibrahim et al.’s [25] study involved comparison between SLIT and SCIT in the treatment of pollen-induced VKC in children; they found no significant difference between both routes.

Our study also showed that single-allergen preparations were clearly more effective than multi-allergen preparations in control of symptoms in both study groups. But since the monosensitized patients were minimal (only 10% of the study population), comparative statistics with polysensitized patients could not be done due to extremely unmatched groups. Kim and colleagues compared multi-allergen SCIT in polysensitized patients with single-allergen SCIT in monosensitized patients with allergic asthma. Mean post-allergen IT symptom scores were significantly ($P < 0.05$) lower than pre-allergen immunotherapy. However, the reduction was significantly less intense in the polysensitized group [36].

IT is tolerated for the vast majority of patients; most reactions were mild, recovered completely within few weeks without any reported complications. The most frequent adverse reaction was local reactions. No systemic or severe adverse reaction was reported.

SLIT has several advantages over SCIT: noninvasiveness, self-administration, and less frequent/severe adverse reactions suggesting that SLIT is a safe and effective treatment modality for patients AC.

In summary; the study reported that aeroallergen polysensitization is common among patients with AC. SPT should be included in the diagnostic workup of these patients. SPT and serum IgE level are very important in identification of IgE-mediated hypersensitivity, detection of the causative allergen and confirmation of the immunological response to therapy. AIT is a safe and effective in controlling symptoms and preventing both exacerbation and development of new sensitizations in patient with AC with no ocular or systemic side effects. It should be considered as an alternative or even a primary treatment for patients with AC to avoid serious ocular side effect of topical steroids, to patients with poor clinical response to medications, to reduce or avoid long-term pharmacotherapy, and also to reduce the economic burden of medications. There is no significant difference between both routes of administration either SLIT or SCIT in achieving clinical and immunologic improvement, so the patient can choose his preferred method for therapy.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in the study were in accordance with the ethical standards of institutional and national research committee and with 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study does not present any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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