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Skin prick test and immunotherapy in children with allergic eye disease

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Aim: To investigate the necessity and efficacy of immunotherapy in children with allergic eye disease.

Materials and methods: The study included 57 patients with allergic eye disease who were followed by the Department of Ophthalmology and Department of Pediatrics at Adnan Menderes University Hospital. Blood and skin prick tests were carried out on 43 patients.

Results: There were 38 male and 19 female patients with a mean age of 11 ± 4 years. The mean follow-up was 31 ± 3 months and 28 ± 4 months in 38 vernal keratoconjunctivitis (VKC) and 19 perennial allergic conjunctivitis (PAC) patients, respectively. Immunotherapy was administered to 8 (42%) PAC patients and 4 (17%) VKC patients. Patients that received immunotherapy did not need further medical treatment for their allergies.

Conclusion: A skin prick test should be considered in the clinical evaluation of an allergic eye disease, especially if it is accompanied by other allergic diseases. Immunotherapy should be considered as a possible treatment option.

Key words: Allergic agents, vernal keratoconjunctivitis, perennial allergic conjunctivitis, skin prick test, immunotherapy

Alerjik göz hastalığı olan çocuklarda prick deri testi sonuçları ve immünoterapi

Amaç: Göz alerjisi bulunan çocuklarda immünoterapinin gerekliliğinin ve etkinliğinin araştırılması.

Yöntem ve gereç: Adnan Menderes Üniversitesi Hastanesi Göz Hastalıkları A.B.D. ve Çocuk Sağlığı ve Hastalıkları A.B.D. tarafından izlenen 57 göz alerjisi olgusu çalışmaya dahil edildi. 43 olguya kan ve prick deri testleri uygulandı.

Bulgular: 57 hastanın 38'i erkek, 19'u kız olup yaş ortalamaları 11 ± 4 olarak bulundu. Sekiz PAK'lı olguya (% 42) ve 4 VKK'lı olguya (% 17) immünoterapi uygulandı. İmmünoterapi uygulanan grupta daha sonra medikal tedaviye ihtiyaç kalmadı.

Sonuç: Göz alerjileri değerlendirilirken, özellikle yandaş alerjik hastalıkların da eşlik ettiği olgularda, prick deri testi uygulanmalı. İmmünoterapinin tedavi seçenekleri arasında yer alabileceği düşünülmelidir.

Anahtar sözcükler: Allerjik ajanlar, vernal keratokonjonktivit, perenial alerjik konjonktivit immünoterapi, prick deri testi

Introduction

Allergic conjunctivitis is one of the most commonly encountered external eye diseases. Extreme conjunctival allergy to a foreign substance results in discharge, redness, itching, foreign body sensation, burning, chemosis, and photophobia. Conjunctivitis can be grouped into 4 main

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categories: perennial allergic conjunctivitis (PAC), vernal keratoconjunctivitis (VKC), atopic keratoconjunctivitis (AKC), and giant papillary conjunctivitis. Autoimmune conjunctivitis occurs in ocular cicatricial pemphigoid and Stevens-Johnson syndrome. Other forms of allergic conjunctivitis can be classified as superior limbic keratoconjunctivitis, ligneous conjunctivitis, and toxic follicular conjunctivitis.

Ocular allergy is estimated to affect 20% of the population on an annual basis and the incidence is increasing (1). Approximately half of the patients have a personal or family history of other allergic conditions such as allergic rhinitis, atopic dermatitis, and asthma (2).

Allergen immunotherapy is effective in patients with allergic rhinitis, allergic conjunctivitis, allergic asthma, and allergic reactions to Hymenoptera venom (3-6). To the best of our knowledge, there is no published article about treating VKC with immunotherapy.

Perennial allergic conjunctivitis is the most common ocular allergic disease. This condition usually begins early in life. There is often a family history of allergy. There may be a personal history of other allergic diseases, such as asthma. In predisposed individuals, airborne environmental antigens (allergens) contact the conjunctival and/or nasal mucosa, stimulating a type I hypersensitivity reaction (a local anaphylaxis). Type I hypersensitivity involves antigen binding to immunoglobulin E (IgE) bound to the surface of mast cells and subsequent cross-linking. This stimulates mast cell degranulation and release of preformed mediators, such as histamine. Histamine and other mediators released by mast cells increase conjunctival microvascular permeability and cause systemic effects such as increased vasopermeability, vasodilatation, and bronchoconstriction. The most important symptom is itching, followed by watery eyes with mild redness. Eye symptoms may be accompanied by nasal symptoms such as rhinorrhea, sneezing, nasal obstruction, itching, and asthmatic-like symptoms.

VKC typically begins in children before puberty and has a tendency to lessen in the second and third decades. In the majority, the onset is before age 10. VKC resolves with age, usually after an interval of 2 to 10 years. In some patients, VKC does not resolve and instead transforms into adult AKC. VKC is a bilateral chronic inflammatory disease of the conjunctiva and cornea. Males are affected 2 to 3 times more frequently than females; however, the prevalence in females increases after puberty and equals that of males after age 20.

VKC involves a type IV hypersensitivity reaction, as well as type I. Inflammation may result in severe vision loss. VKC is commonly found in individuals with a personal or family history of allergic disease or atopy. The most important ocular and common symptom is itching. It is usually seasonal, occurring in the spring and summer; however, some persons are affected year-round. The disease is prevalent in hot, dry climates, especially in the Mediterranean area. The most important sign is multiple giant cobblestone (flat-topped) papillae on the superior tarsal conjunctiva. There is often dense mucus draped over these papillae.

Because mast cells are found in higher numbers in the conjunctiva, the cornerstone of medical therapy is the use of mast cell stabilizers. More severe cases with marked symptoms or corneal involvement may require topical corticosteroids or cyclooxygenase inhibitors. Long-term use of steroids has been associated with a greater risk for glaucoma and cataracts, and other side effects such as irregular menstrual bleeding and growth retardation in children. Immunotherapy, as a form of desensitization, is another option used for the pediatric population with allergic diseases and can be used when it is not possible to avoid exposure to allergens.

The aims of this study were to determine common allergens that cause allergic eye diseases in children using the skin prick test and to determine the efficacy of immunotherapy.

Materials and methods

The study included 57 allergic eye disease patients who were followed by the Department of Ophthalmology and Department of Pediatrics from January 2003 to September 2009 at Adnan Menderes University Hospital, Turkey. The type of allergic eye disease, accompanying allergic diseases in the medical history, family history, beginning day of symptoms,

severity, and seasonal changes were recorded from the files. All of the patients had undergone complete ophthalmologic and pediatric examinations at baseline and follow-ups. Dermatologic and ear, nose, and throat examinations were done when needed. Blood eosinophil percentage was checked in every patient; if it was >3%, it was considered as eosinophilia. Likewise, total IgE levels were measured in every patient, and if the total IgE level was >180 IU/dL, it was considered high. The diagnosis of allergic conjunctivitis was made with detailed ophthalmologic examinations, including a detailed biomicroscopic examination of both the bulbar and palpebral conjunctival areas. A skin prick test was given to 43 patients and was considered positive if the induration was larger than the control by 3 mm or more at 15 min. A larger wheal means greater allergic sensitivity. Immunization was done by injections to the skin. Immunotherapy was applied to 12 (27.9%) of 43 allergic eye disease patients who had the skin prick test. Buffered saline and histamine were used as the control.

The allergens used to detect sensitization in the skin prick tests were as follows (with their companies): grass mix (*Dactylis glomerata*, *Lolium perenne*, *Festuca rubra*, *Poa pratensis*, *Phleum pratense*, *Secale cereale*, *Holcus lanatus*, *Anthoxanthum odoratum*, *Arrhenatherum elatius*, *Agrostis stolonifera*, *Alopecurus pratensis*, and *Festuca pratensis*; ALK, Horsholm, Denmark), tree mix I (*Alnus glutinosa*, *Corylus avellana*, *Populus deltoides*, *Ulmus campestris*, and *Salix caprea*; Allergopharma, Reinbek, Germany), tree mix II (*Betula verrucosa*, *Quercus robur*, *Platanus acerifolia*, and *Fagus sylvatica*; Allergopharma), mold mix (*Aspergillus fumigatus*, *Penicillium notatum*, *Alternaria alternata*, *Mucor mucedo*, and *Cladosporium cladosporioides*; HAL Allergy, Leiden, the Netherlands), and weed mix (*Urtica dioica*, *Plantago lanceolata*, *Artemisia vulgaris*, and *Taraxacum officinale*; Allergopharma).

Results

The demographics, diagnoses, and associated allergic diseases of patients are presented in Table 1. Nineteen patients were found to have PAC and 38 were found to have VKC. Eosinophilia was present in 16 (84%) of the PAC patients, with a mean percentage of 8 ± 3%, and in 29 (76%) of the VKC patients, with a mean percentage of 6 ± 2%. An increased total IgE level was present in 15 (79%) of the PAC patients, with a mean of 775 ± 767 IU/dL, and in 22 (58%) of the VKC patients, with a mean of 410 ± 343 IU/dL.

Skin test results for the PAC and VKC patients are given in Table 2. The highest positive sensitivities of allergens for VKC in the skin prick tests were 70.8%

Table 1. Demographics, diagnosis, and associated allergic diseases of 57 patients.

	PAC	VKC
Number of patients	19	38
Male/female	14/5	24/14
Age (years)	11.00 ± 3.68	9.47 ± 3.65
No accompanying allergic disease	NA	12
Allergic rhinitis	9	13
Asthma	NA	3
Eczema	NA	NA
Allergic rhinitis + asthma	6	8
Allergic rhinitis + eczema	3	2
Allergic rhinitis + asthma + eczema	1	NA

PAC, perennial allergic conjunctivitis; VKC, vernal keratoconjunctivitis.

Table 2. Skin test results for PAC and VKC patients.

Agents	PAC (n = 19)	VKC (n = 24)
Tree pollens	11 (57.9%)	17 (70.8%)
Grass pollens	15 (78.9%)	16 (66.7%)
Festuca	11 (57.9%)	13 (54.2%)
Wheat pollens	16 (84.2%)	17 (70.8%)
Mite	10 (52.6%)	13 (54.2%)
Weed pollens	6 (31.6%)	11 (45.8%)
Molds	3 (15.8%)	10 (41.7%)
Cat	1 (5.3%)	6 (25%)
Cockroach	1 (5.3%)	4 (16.7%)

PAC, perennial allergic conjunctivitis;
VKC, vernal keratoconjunctivitis.

(n = 17) for tree and wheat pollens and 66.7% (n = 16) for grass pollens. The highest positive sensitivities of allergens for PAC in the skin prick tests were 84.2% (n = 16) for wheat pollens and 78.9% (n = 15) for grass pollens.

Most of the patients had an allergic reaction to more than one agent. Only 3 (16%) of 19 PAC patients and 1 (4%) of 24 VKC patients were positive for only 1 of the tested allergens. Five (26%) of 19 PAC patients and 3 (12%) of 24 VKC patients were positive for more than 1 agent.

The distribution of VKC patients who had a skin prick test and immunotherapy is given in Table 3. Seven had no accompanying allergic disease and were not positive for any of the tested allergens, 4 (17%) out of 24 VKC patients who had a skin prick test were positive for at least 1 agent and received systemic immunotherapy, 3 had allergic rhinitis and asthma, and 1 had only allergic rhinitis and accompanying allergic disease (Table 3).

The distribution of PAC patients who had a skin prick test and immunotherapy is given in Table 4. All of the 19 PAC patients had at least 1 accompanying allergic disease and had a skin prick test. Eight (42%) received systemic immunotherapy. As accompanying allergic diseases, 4 had allergic rhinitis, 2 had allergic rhinitis and asthma, 1 had allergic rhinitis and eczema, and 1 had allergic rhinitis, asthma, and eczema (Table 4).

Immunotherapy was applied to 8 (42%) PAC patients and 4 (17%) VKC patients. After a decrease in symptoms and signs, the immunotherapy applied group did not need further medical treatment.

All of the patients who underwent immunotherapy were treated. After 8 months of therapy, itching, photophobia, burning, symptoms of epiphora and conjunctival hyperemia, chemosis, and signs of mucous discharge decreased in all of the patients who had immunotherapy. Moreover, after 1 year of immunotherapy, patients did not need any further antiallergic medications.

Table 3. The distribution of VKC patients who had a skin prick test and immunotherapy.

	Skin prick test	Immunotherapy
Only VKC	7	NA
VKC + allergic rhinitis	6	1
VKC + asthma	1	NA
VKC + allergic rhinitis + asthma	8	3
VKC + allergic rhinitis + eczema	2	NA

PAC, perennial allergic conjunctivitis; VKC, vernal keratoconjunctivitis.

Table 4. The distribution of PAC patients who had a skin prick test and immunotherapy.

	Skin prick test	Immunotherapy
Only PAC	NA	NA
PAC + allergic rhinitis	9	4
PAC + allergic rhinitis + asthma	6	2
PAC + allergic rhinitis + eczema	3	1
PAC + allergic rhinitis + asthma + eczema	1	1

PAC, perennial allergic conjunctivitis; VKC, vernal keratoconjunctivitis.

Discussion

A skin prick test should be considered in the clinical evaluation of an allergic eye disease, especially if it is accompanied by other allergic diseases. In cases where a specific etiology is detected, immunotherapy should be considered as a treatment option.

In this study, the most common accompanying allergic disease among all of the patients (57 patients) with eye allergy (73.7%) was allergic rhinitis (42 patients). As the treatments of allergic rhinitis and PAC were similar, the patients with PAC who previously received medication for allergic rhinitis did not have very serious symptoms or signs in their eyes. Due to relatively tolerable eye symptoms and signs compared with the VKC patients, for the patients with PAC, the main indication for the skin prick test were the accompanying allergic diseases such as allergic rhinitis, asthma, and eczema. In contrast to the PAC patients, the main indication for the skin prick test was serious eye allergy in patients with VKC.

Perennial conjunctivitis defines the occurrence of eye symptoms throughout the year. During seasonal exposure, the patient's symptoms and signs become more prominent, and they might be in need of additional medications such as corticosteroids. These clinical findings are very important to determine. Complete ophthalmologic examinations were given to the patients during each visit. Patients were invited to the clinics every month, although when needed, some visited more frequently.

PAC patients with accompanying allergic disease and VKC patients who were positive for any of the tested allergens received immunotherapy.

Chowdary et al. showed that the total IgE levels in their control group ranged from 10 IU/mL to 380 IU/mL, with a mean of 180 IU/mL (7). IgE levels were measured in every patient to determine atopic tendency before clinical examination to give general information about the patients, and if the total IgE was over 180 IU/dL, it was considered to be high; this was not used to diagnose allergic conjunctivitis.

Immunotherapy provides short- and long-term benefits. Short-term benefits include a gradual decrease in symptoms and signs and cessation of steroids. In the long term, the development of keratoconus in VKC, as well as asthma and eczema, might be avoided.

A skin prick test should be applied to VKC patients with or without any other allergic diseases, and to PAC patients with associated allergic disease. If an allergen is defined, immunotherapy should be planned as a treatment option. Regional variations in the rates of sensitization to inhalant allergens have been shown in several large European studies such as the European Community Respiratory Health Survey (ECHRS), the International Study of Asthma and Allergies in Childhood (ISAAC), and other multicountry studies. Currently, there is no published review summarizing the data for Europe. Furthermore, harmonization of skin prick testing across Europe is desirable for both the purpose of clinical practice as well as for clinical research. This

should be in terms of the choice of a standard panel of allergens, the source of extracts or use of molecular standards, and the technical procedure of testing.

Aside from seeing pediatricians, children with ocular allergies should consult an ophthalmologist to define whether they have PAC or VKC and if they need a skin prick test and immunotherapy.

These results will aid in etiology research and the search for treatment alternatives of allergic eye diseases in children. The skin prick test has some advantages, such as being simple, relatively painless, and inexpensive; providing immediate results; and offering the ability to test several allergens simultaneously. After a decrease in symptoms and signs, the immunotherapy-applied group did not need further medical treatment.

The skin prick test is a standardized clinical test that is applied in pediatric allergy clinics. Unfortunately, immunotherapy is not a sought-after treatment option for allergic eye diseases. Our purpose was to raise awareness of a successful treatment option for allergic eye diseases, especially when accompanied with other allergic diseases.

The low number of the patients is a limitation of this study. Further studies with a higher number of patients and with a longer follow-up (more than 3 years) are needed. It is suggested that all patients with ocular allergic diseases should undergo an ophthalmic evaluation to facilitate a differential diagnosis. A skin prick test should be considered in the clinical evaluation of an allergic eye disease, especially if it is accompanied by other allergic diseases. In cases where a specific etiology is detected, immunotherapy should be considered as a viable treatment to decrease symptoms and signs as well as to allow the possible withdrawal of medical treatment.

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