

The Development of Hypersensitivity to New Allergens in Allergic Rhinoconjunctivitis Patients Who Do Not Respond to Specific Immunotherapy

SPESİFİK İMMÜNO TERAPİYE CEVAP VERMEYEN ALLERJİK RİNOKONJUKTİVİTLİ HASTALARDA YENİ ALLERJENLERE KARŞI HİPERSENSİTİVİTE GELİŞİMİ

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Summary

//; this study, 129 patients (38 male, 91 female; mean age:34.6 years) with allergic rhinoconjunctivitis (AR) were diagnosed with clinical features, evaluation of total and specific IgE levels in sera, positive skin prick test and positive conjunctival provocation test were given specific immunotherapy (SIT) for 3 years. We re-evaluated all patients with skin prick test and serum total and specific IgE levels after SIT. Additionally, we determined symptom scores for each patient before and after from SIT. We found that 78 of the patients (59.5 %) were sensitive to grass pollens, 38 of the patients (29 %,.) were sensitive to house dusts and 15 of the patients (11.5 %) were sensitive to herb pollens. We aimed to evaluated cause of failure in patients with AR who were given SIT for three years but had been unsuccessful.

In 43 of 129 patients, hypersensitivity reactions to new allergens were detected that were not determined in the beginning of SIT. There were no expected reduction in neither symptom scores nor in the need of antihistaminic usage during SIT in these patients. We ascertained hypersensitivity to herb mix allergens in 22 patients (51 %), tree mix allergens in 16 patients (37.2 %), D. fdrinae and pteronyssinus in 11 patients (25.5 %), animal dendars in 7 patients (16.2 %), grass mix allergens in 2 patients (4.6 %) and mould allergens in one patients (2.3 %).

As a result, we emphasize that if there is no expected clinical improvement we should consider hypersensitivity to other allergens in AR patients who received SIT.

Key Words: Allergic rhinoconjunctivitis,
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Özet

Bu çalışmada klinik (kellikleri, serum total ve spesifik IgE seviyeleri, pozitif cilt prick testi ve pozitif konjunktival provokasyon testi (KPT) ile allerjik rinokonjunktivit (AR) tanısı konulan 129 hastaya (38 erkek, 91 kadın; ortalama yaş: 34.6 yıl) 3 yıl boyunca spesifik inmiinoterapi (SİT) uygulandı. SİT sonrası tüm hastaları cilt prick testi ve serum total ve spesifik IgE seviyeleri ile yeniden değerlendirdik. Ayrıca her bir hasta için SIT öncesi ve sonrasında semptom skorlarını belirledik. SİT başlangıcında 78 hastada (% 59.5) grass polenlere, 38 hastada (% 29) ev tozlarına ve 15 has/ada (% 11.5) herb polenlere karşı hassasiyet saptandı. Çalışmada SİT'ye umulan cevabı vermeyen hasta/ardaki yetersiz cevabın nedenlerinin araştırılması amaçlandı.

SİT' hin başlangıcında saptanmayan yeni allerjenlere karşı hassasiyet gelişimi 129 hastanın 43'ünde saptandı. Bu hasta/arda SİT esnasında ne semptom skorunda ne de antihistaminik kullanımında umulan azalma yoktu. Bu hastaların 22'sinde (% 51) herb miks allerjenlere, 16'sında (% 37.2) tree miks allerjenlere, 11'inde (% 25.5) D. farinae and pteronyssinus ullaerjenlerine, 7'sinde (% 16.2) hayvan tüylerine, 2'sinde (% 4.6) grass miks allerjenlere ve bir hastada (% 2.3) mould allerjenlere karşı hassasiyet saptandı.

Sonuç olarak SİT uygulanan AR' li hastalarda, eğer umulan klinik düzelme görülüyorsa diğer allerjenlere karşı hipersensitivite gelişimi düşünülmelidir.

Anahtar Kelimeler: Allerjik rinokonjunktivit.
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Allergy is usually considered to be an immunologic dysfunction leading to a severe local inflammatory response or to more serious systemic effects. Such effects are brought about by contact with allergens which, during prior exposure of the

patient, have induced particular elevated specific immune responses, in most cases, of the IgE isotype (1). Allergic rhinoconjunctivitis (AR) is characterized by nasal irritation, sneezing, lacrimation, itching, conjunctival hyperemia and rhinorhea following exposure to the relevant allergen (2,3).

Specific immunotherapy (SIT) has been widely used to treat immediate hypersensitivity type reactions that known to be primarily mediated by allergen specific IgE antibodies, such as allergic rhinoconjunctivitis, asthma and severe reactions to insect stings (4-6). An early classic evaluation of the efficacy of SIT was reported by Lowell and Franklin in 1963 (7). Multiple studies by various investigators have demonstrated decreased symptoms resulting from SIT, however, the effect of SIT is not clear on immune system (8).

In most instances, correctly performed specific allergen immunotherapy is a safe and effective therapeutic modality. It is easy to administer and in most patients is well tolerated. Some patients do not respond to SIT. Cause of this may be incorrect diagnosis, insufficient treatment and development or aggravation of other allergies (6,8-12).

In this study, we aim to evaluate why therapy was unsuccessful in some patients with AR who has been applied SIT.

Materials and Methods

In this study, 129 patients with AR were diagnosed with personal and family history, physical examination, positive skin prick test, positive conjunctival provocation test and in vitro tests such as serum levels of total and specific IgE antibodies were admitted. Ninety-one patients (70.5%) were female and 38 patients were men (29.5%) with mean age were 34.6 ± 7.8 years (mean \pm SD) (range 19-56).

3 Hep / ml (histamine equivalent prick/ml) allergen dose was used for prick test and allergens that the patients are sensitive were determined. Skin prick tests were read at 15 min. The reactions were graded as follows : + corresponding to a reaction of one-fourth the histamine standard, ++ reaction half the size, +++ equal to, and ++++ twice as large as the wheal of the histamine standard (10 mg/ml). Reactions > ++ were regarded as positive.

The allergens used for skin prick test and conjunctival provocation test were provided by A L K . We found hypersensitivity to grass pollens in 76 patients (58.9%), to dermatophagoides pteronyssinus and dermatophagoides farinae in 38 patients (29.5%) and to herb pollens in 15 patients (11.6%). Each patients were sensitive only one allergen and have not another disease.

Hyposensitization was started with weekly injections and the allergen dose was increased as rapidly as possible until a maximal tolerated dose was reached (maximal dose: 100.000 SQU (Standard Quantification Unite)/ ml). The patients were applied SIT with allurad antigens of A L K for three years and were re-evaluated with skin prick test after three years.

Symptom score (SS) was evaluated with following criteria; rhinorhea, nasal obstruction, sneezing and itching at nose and palate. Each symptom were graded as; 0: no symptom, 1+ : mild, 2+ : moderate, 3+ : severe symptom. Total symptom scores were calculated in each patient before and after SIT. Less than 50 % decreases in SS were accepted as good clinical response to SIT.

Serum specific and total IgE levels were determined by fluoroimmunoassay (using FEIA kit, Pharmacia CAP system).

Statistical analyses were performed by student T test.

Results

In the beginning of the SIT, we found that 76 of the patients (58.9%) were sensitive to grass pollens, 38 of the patients (29.5 %) were sensitive to D. pteronyssinus and D. farinae and 15 of the patients (11.6%) were sensitive to herb pollens.

The symptom score was evaluated before and three years after SIT in every patient. A decrease more than 50% in symptom score was accepted as positive response to therapy. According to that, 95 of patients (73.6%) responded to therapy, where as 34 (26.4%) did not.

In 43 of 129 patients (33.3%), hypersensitivity reactions were established to new allergens that were not determined in the beginning of SIT. Twenty eight of these patients were female and 17 patients were male (mean age \pm SD: 32.3 ± 6.1

years). According to sex and age, there was no statistical difference between patients responded and who did not respond to SIT ($p > 0.05$).

There were no expected reduction in neither symptom scores nor in the need of antihistamine usage during SIT in these patients. Although SS was decreased more than 50% in 9 AR patients (6.9%), we determined hypersensitivity reactions to new allergens in these patients. In 5 of 43 patients (11.6%), hypersensitivity reactions to allergens were established for more than one antigen. In the end of the SIT, we determined new hypersensitivity reactions to; herbs mix allergens in 22 patients (51%), tree mix allergens in 16 patients (37.2%), D. farinac and pteronyssinus in 11 patients (25.5%), animal danders in 7 patients (16.2%), grasses mix in 2 patients (4.6%), mould allergens in one patients (2.3%).

Discussion

Inhaled allergens are important factors in the etiology and provocation of allergic rhinoconjunctivitis. It is a matter of debate why some of the people living in the same region have Type I hypersensitivity reaction and why some have not. In this aspect, genetic and environmental factors are both involved (4,5,13,14). Allergy is common disease which have a high prevalence in most human populations and show a clear familial aggregation (1,13).

Since Noon's report in 1911 (15), SIT has been widely accepted as a specific treatment for allergic diseases such as allergic rhinoconjunctivitis, asthma and severe reactions to insect stings and has been shown to be clinically effective in numerous controlled trials (5,8,16-19). Allergen immunotherapy is effective only in IgE-mediated allergic diseases. Such therapy consist of injecting increasing amounts of the offending allergens to the patient to bring about reduced sensitivity to the allergens (4,6,9). While the exact mechanism by which SIT causes this reduction in symptoms is unclear, many immunologic changes has been documented to occur in patients receiving this therapy. Several possibilities have been proposed, including altered regulation of IgE synthesis, production of specific IgG4 as blocking antibodies, decreasing of degranulation in mast and basophil cells as a result to allergen and

stimulation of T lymphocytes that can suppress production of IgE (6,20-23).

SIT is relatively easy to administer and in the majority of patients it is well tolerated. The SIT usually relieve symptoms of the patients who are candidate for this therapy, however, it does not necessarily result in cure (4-6).

SIT is a long-term treatment and optimal length of treatment is unknown. Usually a treatment period of at least 3 to 5 years is recommended. Treatment may be unsuccessful because of incorrect diagnosis, insufficient allergen dosage, and the development or aggravation of other allergies. In addition, a proportion of patients do not respond to immunotherapy. In general, patients with multiple unrelated sensitivities, e.g. to pollens, dust mites, animal danders, and moulds, have more severe or more complex disease and do less well on this form of therapy (6).

Therefore, patients who have only one allergen hypersensitivity were included to this study. We evaluated symptom scores and need of antihistaminic usage in each patient along three years, and repeated skin prick test at the end of the treatment. We specially determined development of new allergen hypersensitivity in patients who do not respond to SIT. We thought that the cause of unsuccessful treatment is development of new allergen hypersensitivity in some patients with AR.

In our study, 73.4% of patients were successfully treated with the SIT. This result is in correlation with other studies in literature (5,7,24,25). Consequently, SIT is an effective and safe therapeutic method in AR therapy. However, if there is no expected clinical recovery in AR patients who applied SIT, we should consider hypersensitivity to other new allergens.

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