

The Evaluation of Local and Systemic Reactions to Subcutaneous House Dust Mite Allergen Immunotherapy

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ABSTRACT

Objective: Allergen-specific immunotherapy is an effective treatment method that enables the development of immunotolerance against allergens in allergic rhinitis, asthma, and venom allergy. This study investigated the local and systemic reactions during subcutaneous house dust mite allergen immunotherapy.

Methods: Injection-related local and systemic reactions of 45 patients who received subcutaneous mite immunotherapy were evaluated retrospectively.

Results: Forty-five children, 15 (33.3%) females and 30 (66.4%) male were included in the study. A total of 582 injections were administered. A local reaction was observed in 23 (3.94%) of all injections and the systemic reaction was observed in only 1 (0.17%) injection. Sixteen (37.7%) of the children had local reactions during the immunotherapy process and 1 (2.2%) had a systemic reaction.

Conclusion: Although subcutaneous mite immunotherapy is a safe treatment, it should only be applied in centers with appropriate emergency equipment and trained healthcare professionals due to possible systemic reactions.

Keywords: Allergy, house dust mite, immunotherapy, local reaction, systemic reaction

INTRODUCTION

Allergen-specific immunotherapy (AIT) is a treatment method that provides immunotolerance by application of responsible allergens at specific doses and intervals.¹ It is an effective treatment for IgE mediated allergic diseases such as asthma, allergic rhinitis and venom allergy. Nowadays, AIT is available in subcutaneous, sublingual, oral, epicutaneous, and intralymphatic forms.^{1,2} AIT is considered a safe treatment when performed in experienced centers and with appropriate indications. The most frequent side effects of AIT are local reactions such as edema or erythema, but systemic side effects could be observed.²

House dust mites (HDM), to *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, are common indoor allergens and they are associated allergic rhinoconjunctivitis, allergic asthma,

atopic dermatitis. Eighty-two different allergens from 10 different mite species have been identified.^{3,4} In North and South America, Europe, Southeastern Asia, and Australia, 85% of the asthma cases showed HDM sensitivity and in middle China, this ratio is 91.1%.^{3,5,6} About 50% of pediatric and adolescent asthma cases showed HDM allergen sensitivity.⁷

The effect of protective environmental measures is limited in HDM allergy and in most cases, additional treatment approaches are indicated. HDM immunotherapy is the most effective method in both asthma and allergic rhinitis treatment.⁸⁻¹¹

This study aimed to evaluate the local and systemic side effects in the children with asthma or allergic rhinitis who received HDM subcutaneous immunotherapy (SCIT).

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MATERIALS AND METHODS

In this retrospective study, the medical records of the children diagnosed with allergic rhinitis or asthma who received SCIT for HDM and followed in the Pediatric Allergy Department between January 2020-January 2021 were evaluated. From the patient’s records, demographic variables, clinical and laboratory findings were obtained. Also, adverse effects after SCIT applications were recorded. According to World Allergy Organisation recommendations, adverse SCIT reactions are classified into 2 categories; local and systemic reactions.¹² Systemic reactions can range in severity, from mild to life threatening anaphylaxis. Local reaction was defined as swelling, pruritus and redness at the injection site. Also, local reactions can be classified according to size and duration of occurrence. An extensive local reaction occurs when a local reaction develops at an injection site that is larger than the size of the patient’s palm, and minor local reaction is smaller than as well. Induration developing within the first 30 min was accepted as an early local reaction, and induration developing after 30 minutes was considered a late local reaction.¹²

Eleven children were under antihistaminic prophylaxis before injection. They were prescribed antihistaminic due to previous history of recurrent local reactions.

HDM SCIT protocol applied according to the European Academy of Allergy and Clinical Immunology guidelines.¹³

Ethical board approval was obtained from the Institutional review board of the Uludağ University Faculty of Medicine (approval number: (2022-4/54 , date: 23.02.2022).

Statistical Analysis

All statistical analysis was performed using IBM SPSS for Windows, version 23 (IBM Corp., Armonk, NY). The mean, median, minimum, maximum, and standard deviation (SD) values were used to describe data. Kolmogorov-Smirnov normality test was used to analyze the distribution of data. Chi-square or Fisher’s exact tests were used in the comparison of qualitative data. A p-value <0.05 was considered as statistically significant.

RESULTS

A total of 45 children, 15 (33.3%) females, and 30 (66.4%) males were included in the study. According to the skin prick test results of the patients, 33 (73.3%) were defined as monosensitized and 12 (26.4%) were polysensitized. Thirty-eight (84.4%) of the patients were receiving HDM SCIT only and 7 (15.6%) had multiple SCIT in the form of HDM and pollens.

A total of 583 injections were administered. Local reactions were observed in 23 (3.94%) of all injections 21 early local reactions, 1 early large, 1 late large local reaction and 1 (0.17%) systemic reaction.

Four (1.16%) local reactions were observed in 344 injections of the build-up phase. Nineteen (7.9%) local reactions were observed in

239 injections of maintenance phase. Only one systemic reaction was observed in the maintenance phase of SCIT (Table 1).

According to the gender of the children, late minor local reactions were more common in females than in males (p=0.004) (Table 2). The local reaction frequency was significantly lower in children using antihistamine prophylaxis (Table 3). The frequency of reactions was similar in children with and without asthma, allergic rhinitis, and conjunctivitis.

During the immunotherapy, 17 (37.7%) of the children had local reactions and only 1 (2.2%) had a systemic reaction. One child with asthma had a systemic reaction with a sudden onset of shortness of breath and bronchospasm 10 min after the administration of SCIT.

Eleven children were under antihistaminic prophylaxis before injection. Of those, two had early minor, one of them had late minor, and 2 had late extensive local reactions. Thirty-four patients did not require antihistamine prophylaxis.

DISCUSSION

Allergen immunotherapy is defined as “the only treatment method that can change the natural course of allergic diseases”.¹⁴ In SCIT, mild-to-moderate systemic reactions occur in approximately 0.1% of patients, while severe reactions are rare (1 in 1 million injections).⁶

In the previous studies, local reactions were reported in 5.2% to 82% of patients during the immunotherapy process, and systemic reactions were reported between 0.06% and 3.2%.¹⁵⁻¹⁸ studies conducted in Turkey reported that local reactions occur in 0.38-4% of all injections and systemic reactions occur in 0.1% to 0.2%.^{19,20} In a study evaluating HDM SCIT injection in children,

Table 1. The frequency of reactions after injection

Immunotherapy phases	Number of injection n (%)	Local reaction n (%)	Systemic reaction n (%)
Build-up	344	4 (1.16%)	0
Maintenance	239	17 (7.9%)	1 (0.4%)
Total	583	23 (3.94%)	1 (0.17%)

Table 2. Distribution of patients who had local and systemic reactions by gender

Type of reaction	The number of patient		p-value
	Female	Male	
Early minor local reactions	0	2	-
Early extensive local reaction	0	0	-
Early systemic reaction	1	0	-
Late minor local reaction	9	4	0.004
Late extensive local reaction	1	1	0.55
Late systemic reaction	0	0	-

Table 3. Distribution of patients who had reactions according to being under antihistamine prophylaxis			
Type of reaction	Under antihistamine prophylaxis (n=11)	Not under antihistamine prophylaxis (n=34)	p-value
Early minor local reactions	2	0	-
Early extensive local reaction	0	0	-
Early systemic reaction	0	1	-
Late minor local reaction	1	12	0.040
Late extensive local reaction	2	0	-
Late systemic reaction	0	0	-

3.5% local and 0.1% systemic reactions were observed. Most of the systemic reactions were associated with the respiratory system.²¹ Sasihüseynoğlu et al.²² reported the data of 303 patients who underwent SCIT with a local reaction developed in 54 (17.8%) patients and systemic reaction in 4 (1.3%) patients. Local reactions were more common in those receiving HDM SCIT (20.6%) than in those receiving grass pollen immunotherapy (16.7%). Additionally, systemic reactions have been reported only in HDM SCIT.²² Consistent with the literature, in our study, local reactions were observed in 23 (3.94%) of all injections and systemic reactions were observed in 1 (0.17%). A systemic reaction was observed in a patient during the maintenance phase.

Various studies support the idea that the individual dose of AIT after an extensive local reaction cannot predict the development of systemic reactions. However, there is no evidence that local reactions precede to systemic reactions.^{15,23} The rate of extensive local reaction was found to be almost four times higher in patients who experienced a systemic reaction compared to those who did not experience any systemic reaction.²⁴ Systemic reactions are generally encountered during dose escalation (especially in “rush,” and “clustered” protocols) and mostly non-fatal reactions. Most post-injection systemic reactions occur within the first 30 min. Therefore, patients are expected to wait for at least 30 min after subcutaneous administration.^{1,25}

The principal limitation of this research was that the limited number of patients makes it difficult to provide a definite interpretation. In particular, the findings of this study should be interpreted with caution since they cannot be used to infer causality because of the study design.

CONCLUSION

HDM SCIT is the only treatment modality that can provide a cure for many years for treating asthma and allergic rhinitis. After SCIT injections, patients should be observed for at least 30 min in terms of local and systemic reactions. According to the knowledge gain from this study, systemic reactions are unpredictable so AIT should be administered by an experienced allergy specialist in a setting that permits the prompt recognition and management of adverse reactions.

Ethics

Ethics Committee Approval: Ethical board approval was obtained from the Institutional Review Board of the Uludağ University Faculty of Medicine (approval no: 2022-4/54, date: 23.02.2022).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Z.K., Ş.Ç., Y.H.Ş., Y.C., N.S., Design: Z.K., Ş.Ç., Y.H.Ş., Y.C., N.S., Data Collection or Processing: Z.K., Ş.Ç., Y.H.Ş., Y.C., N.S., Analysis or Interpretation: Z.K., Ş.Ç., Y.H.Ş., Y.C., N.S., Literature Search: Z.K., Ş.Ç., Y.H.Ş., Y.C., N.S., Writing: Z.K., Ş.Ç., Y.H.Ş., Y.C., N.S.

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