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Original Article

Evaluation of demographic data and laboratory of children receiving subcutaneous venom immunotherapy

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Abstract

Aim: Allergic reactions that develop after venom can be serious and fatal. The only treatment that can prevent these serious reactions is venom immunotherapy. Studies on venom immunotherapy in paediatric patients are limited. Aim of this study to evaluate the demographic data and laboratory results of paediatric patients who have received venom immunotherapy.

Materials and Methods: The study included 45 patients who have received subcutaneous venom immunotherapy in Department of Paediatric Allergy and Immunology.

Results: Thirty-three of the patients (73.3 %) were boys and 12 (26.7 %) were girls, the median age was 14 years (min.: 6, and max. 18). *Apis mellifera* venom was given to 24 (53.3 %) of 45 patients, and *Guapes* species venom immunotherapy was given to 21 (46.7 %) patients. While 15 (33.3 %) patients who received immunotherapy were living in Malatya, 30 patients were living in various provinces of the Eastern Anatolia region. While wide local reaction developed in 15 (33.3%) of the patients, systemic reaction developed in 3 (6.7 %) patients during venom immunotherapy. *Apis mellifera* prick test median diameter was determined as 4 mm and median of *Apis* specific Ig E value was determined as 6 kU/L. Guapes species prick test median diameter was determined as 4 mm and median of Guapes specific Ig E value was determined as 4 kU/L.

Conclusion: Immunotherapy with *Apis* venom was more than *Guapes* venom in current study. Large local reaction was observed in 1/3 of the patients during immunotherapy. Therefore, attention should be paid in terms of systemic allergic reactions and large local reactions during immunotherapy. All necessary precautions should be taken during the immunotherapy.

Keywords: Anaphylaxis; immunotherapy; venom allergy

INTRODUCTION

Approximately 56 % to 94 % of the world's population is exposed to insect stings by *Hymenoptera species* at least once in their lifetime (1). Venom allergies that occur as a result of the sting of the bees of the *Hymenoptera species* are the most common reasons for wide local reactions and systemic sting reactions in the clinic. Wide local reaction is defined as a swelling that lasts longer than 24 hours and exceeds 10 cm in diameter (2). Wide local reactions are observed in 2.4% - 26.4% of the population (3). Systemic reactions can cause mild forms of general skin symptoms such as rash, urticaria and angioedema, moderate dizziness, shortness of breath and nausea. In severe forms, it may cause a shock and loss of consciousness, or even cardiac or respiratory arrest. Serious reactions are life threatening and may cause death. The frequency of systemic reactions in epidemiological studies ranges from 0.3 % to 7.5 % in adults and up to 3.4 % in children (4-5).

Venom immunotherapy is the only treatment option that can prevent systemic reactions that occur as a result of bee stings. Immunotherapy is the only treatment method for venom allergies and is used in patients who have had systemic allergic reactions previously caused by bee stings, but who have positive venom diagnostic test reactions (6). Studies performed showed that venom immunotherapy is effective in reducing subsequent systemic reactions in both children and adults. Its effectiveness varies between 77 % and 84 % in immunotherapy with honey bee venom and between 91 % and 96 % in immunotherapy with *Wasp* venom (7-8).

Allergic reactions that may occur during venom immunotherapy are usually in the form of local reactions. The frequency of life-threatening systemic reactions ranges from 0.1 % to 0.2 % (6-9). Although the side effects that can be seen during venom immunotherapy are well known in adult patients, data on children are limited (9-11).

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In this study, we aimed to present the demographic data, laboratory results, diagnostic test results for venom allergy, type of venom immunotherapy, and side effects of subcutaneous venom immunotherapy in our clinic.

MATERIALS and METHODS

In this study, the files of 50 patients who received subcutaneous venom immunotherapy in Inonu University Faculty of Medicine, Department of Pediatric Allergy and Immunology between January 2014 and December 2019 were retrospectively analyzed. Five patients who did not receive venom immunotherapy regularly or did not complete the treatment period were excluded from the study.

From the files data, following information's were recorded; age and gender information, clinical signs and symptoms after insect sting, kind of bee, serum total Ig E level and eosinophilia, results of allergen skin test and serum specific Ig E results for venom, history of atopic disease and history of family venom allergy.

Diagnosis of venom allergy was made according to the recommendations of the European Academy of Allergy and Clinical Immunology (12). All patients had a positive result for allergen skin test and/or serum specific Ig E test (> 0.35 kU/L). Diagnostic tests (allergen skin tests/ serum specific Ig E test) were performed at least 4 weeks after the systemic reaction that occurred due to bee sting (12). Histamine was used for positive control and saline solution was used for negative control. For skin testing, venom extracts (100% *A. mellifera* or *Vespula species*; Alutard SQ, ALK, Hørsholm, Denmark) were performed to the patients epidermally and intradermally at concentrations of 10, 100 and 100 ng/ml, respectively. For intradermal test venom extracts solutions (100% *A. mellifera* or *Vespula species*; Alutard SQ, ALK, Hørsholm, Denmark) were diluated as 10% and 1% concentration. Allergen skin test was considered as positive when mean swelling diameters relative to negative control were at least 3 and 5 mm, in epidermal and intradermal respectively (12).

Traditional subcutaneous venom immunotherapy was initiated in our patients diagnosed with venom allergy with an extract containing the venom species to which our patients were sensitive (100% *A. mellifera* or *Vespula species*; Alutard SQ, ALK, Hørsholm, Denmark). In the initial phase of the treatment, patients were injected with a venom extract of 3-8 µg/dose. Then, the amount of venom extract performed was increased weekly, and the maintenance phase was reached in approximately 6 months. In the maintenance phase, subcutaneous immunotherapy was completed to a total of five years with injections made every 4-6 weeks (13-15).

Side effects that occurred in patients during the immunotherapy phase were noted on the patient's immunotherapy cards. Reactions larger than 10 cm in diameter were considered as wide local reactions and reactions smaller than 10 cm as local reactions during a bee sting. Urticaria, angioedema and findings related to other systems were considered as systemic reactions.

Scientific Research and Publication Ethics Committee approved for study (2021/1538). In addition, written consent form was taken from the patients and/or their parents.

Statistical Analysis

Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS) 20.0 software (SPSS Inc., Chicago, IL). Normality was evaluated by the Kolmogorov-Smirnov test. Descriptive statistics were expressed as the frequency and percentage for categorical variables, whereas quantitative data were expressed as mean (±SD) for normally distributed data and median (min-max) for non-normally distributed data.

RESULTS

Forty-five paediatric patients who were started subcutaneous venom immunotherapy and whose treatment was completed were included in the study. Thirty-tree of the patients (73.3 %) were boys and 12 (26.7 %) were girls. While 15 (33.3 %) patients who received venom immunotherapy were residents of Malatya province, thirty patients were living in various provinces of the Eastern Anatolia region. The median age of the patients was found to be 14 years (min.: 6, max.: 18). Of the 45 patients, 24 (53.3 %) were treated with *Apis mellifera* venom and 21 (46.7 %) were treated with *Guapes* species venom. All of the patients who started immunotherapy had a history of anaphylaxis after bee sting. All of the patients included in the study had received immunotherapy regularly for 5 years (Table 1).

In the evaluation of patients, who received venom immunotherapy, in terms of other allergic diseases; it was determined that 8 (17.8 %) patients had a history of asthma, 4 (8.9 %) patients had a history of atopic eczema, 2 (4.4 %) patients had a history of allergic rhinitis and 1 (2.2 %) patient had a history of food allergy (egg). Twenty-one patients (46.7 %) had a family history of venom allergy.

In the laboratory examination of the patients, 31 (68.9 %) of the patients had eosinophilia and the median total Ig E value was found as 240 kU/L (min.: 27, max.: 1970). In patients who received immunotherapy with honey bee venom, *Apis mellifera* prick test median value was determined as 4 mm (min.: 3, max.: 8) and the median of *Apis mellifera* specific Ig E level was determined as 6 kU/L (min.: 1, max.: 100). In patients who received immunotherapy with wasp venom, *Guapes species* prick test median value was determined as 4 mm (min.: 3, max.: 8) and median of *Guapes species* specific Ig E value was determined as 4 kU/L (min.: 2, max.: 140) (Table 1).

During the immunotherapy, no reaction was observed in 23 (51.1 %) patients, while 4 (8.9 %) patients had local reaction, 15 (33.3 %) patients had large local reaction and 3 (6.7 %) patients had systemic reactions (all of the patients had generalized urticaria).

In the follow-up after venom immunotherapy, 24 patients were exposed bee sting. Thirteen of these patients (54.2 %) had no allergic reaction after bee sting. Large local reaction

was observed in 9 patients (37.5 %) and anaphylaxis was developed in 2 patients (8.3 %) after bee sting.

Table 1. Demographic Data and Laboratory Results of Paediatric Patients Who Have Received Subcutaneous Venom Immunotherapy

	n	(%)
Gender		
Male	33	73.3
Female	12	26.7
Age, median (min-max), years	14	(6 -18)
Province of residence		
Malatya	15	33.3
Other provinces	30	66.6
Type of Immunotherapy		
Apis mellifera	24	53.3
Guapes vespula	21	46.7
Eosinophilia	31	68.9
Median serum total Ig E value (min-max), (kU/L)	240	27-1970
***Apis mellifera* median prick diameter (min-max),** (mm)	4	3-8
***Apis mellifera* median serum specific Ig E value (min-max),** (kU/L)	6	1-100
***Guapes vespula* median prick diameter (min-max),** (mm)	4	3-8
***Guapes vespula* median serum specific Ig E value (min-max),** (kU/L)	4	2-140

DISCUSSION

Bee stings can cause allergic reactions of varying severity both in adults and in children. Patients with severe systemic reactions may experience shock and loss of consciousness, or even cardiac or respiratory arrest. The frequency of these severe reactions can reach up to 4 % in children. Venom immunotherapy should be initiated in patients who have a history of systemic allergic reaction due to bee stings and who have positivity of allergen skin test and/or serum specific Ig E for venom (6). All of our patients who were undergone venom immunotherapy had history of anaphylaxis after a bee sting had sensitivity to venom.

Of the 45 patients we treated with venom immunotherapy, 24 (53.3 %) were treated with *Apis mellifera* venom and 21 (46.7 %) were treated with *Guapes* venom. The reason of the higher number of patients receiving immunotherapy with *Apis mellifera* venom is due to the prevalence of honey beekeeping in Malatya and Eastern Anatolia region.

Various allergic reactions can be seen in patients during venom immunotherapy. These reactions are usually local reactions at the injection site. During immunotherapy, life-threatening systemic reactions are less common than local reactions (6-8). In our study, out of a total of 45 patients, 4 (8.9 %) had a local reaction, 15 (33.3 %) patients had a large local reaction, and 3 (6.7 %) patients had a systemic reaction during the treatment period. In a total of 23 (51.1 %) patients, no reaction was observed during the treatment. Therefore, patients who are started immunotherapy, patient and their parents should be informed about allergic reactions due to immunotherapy.

In the previous studies, it has been shown that venom immunotherapy is effective in reducing subsequent systemic reactions in both children and adults (16). In various studies, the efficiency rate ranges from 77 % to 96 % (7-8). In our study, out of 45 patients whose immunotherapy period was completed, only 2 patients had systemic reactions after a bee sting, which shows that the effectiveness of the treatment is high. Systemic reaction had developed after bee sting in all patients before treatment.

While reviewing the patient files, it was determined that 5 out of 50 patients discontinued venom immunotherapy (10 %). Therefore, the importance of venom immunotherapy should be explained properly to the patients and their parents. It should be emphasized that this treatment is the only method to prevent serious systemic reactions that may develop after a bee sting.

LIMITATIONS

There are few limitations in current study. Firstly, 10 % of the patients loose the follow-up and this condition may have affected our results. Secondly, the small number of patients in our study may affect the generalizability of our results. Thirdly, we did not investigate mastocytosis and could not measure serum tryptase level. Therefore, more studies with pediatric patients are needed.

CONCLUSION

As a result, bee sting cause serious systemic reactions, threatening life in children as well as adults. Venom immunotherapy is the only treatment that prevents systemic reactions that may develop after a bee sting. Therefore, patients with a history of systemic reactions should be directed to allergy clinics for venom immunotherapy. Large local reaction was observed in 1/3 of the patients during immunotherapy. Therefore, attention should be paid in terms of systemic allergic reactions and large local reactions during immunotherapy. All necessary precautions should be taken during the immunotherapy. In addition patients/parents are informed about the allergic reactions that may develop during the treatment.

Competing Interests: The authors declare that they have no competing interest.
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