

Efficacy of Allergen Immunotherapy in the Treatment of Chronic Spontaneous Urticaria

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Abstract

Introduction: In most patients, the cause of chronic urticaria is unknown. Aeroallergens may potentially cause chronic urticaria. This study was conducted to investigate the clinical efficacy of immunotherapy in patients with chronic spontaneous urticaria.

Methods: Patients diagnosed with chronic spontaneous urticaria and receiving subcutaneous allergen-specific immunotherapy for at least 6 months duration were enrolled. Demographic data, allergen sensitization patterns from skin prick test, urticaria activity score, angioedema activity score, and medication scores were recorded. The scores recorded were measured before and after allergen immunotherapy.

Results: There was a significant decline in activity and medication scores ($p < 0.0001$). 25% of studied patients had complete improvement in hives score and 15.6% in itching score. However, 43.5% and 42.9 % of them had complete improvement in the angioedema and medication scores respectively. Sensitization patterns were not associated with improvement in activity scores.

Conclusion: immunotherapy is effective in patients with chronic spontaneous urticaria. No relationship was detected between sensitization patterns and symptom improvement.

Keywords: allergen immunotherapy; chronic spontaneous urticaria; allergen sensitization

Introduction

Chronic urticaria is identified by itching and hives with or without angioedema, for more than 6 weeks. The disease makes considerable psychological and financial problems for the patient in addition causes a journey between physicians of different specialties [1]. Chronic urticaria is divided into chronic inducible urticaria (CIU) and chronic spontaneous urticaria (CSU). Histamine, which is secreted by mast cells, is crucial in the pathophysiology of Chronic urticaria. The treatment of chronic urticaria is mostly symptomatic and comprises antihistamines which do not control the condition in many cases, and more extensive therapy is required [2]. Omalizumab, a monoclonal antibody to IgE has been employed as a highly successful treatment. Despite its efficacy, recurrence of CSU with omalizumab therapy is commonly reported [3,4]. In most patients, the cause of chronic urticaria is unknown. Medications, foods, infections, and autoimmune are among the agents and variables implicated in causing urticaria symptoms [5]. Aeroallergens may potentially cause chronic urticaria. Some allergens may break the epidermal barrier and immediately stimulate nerve

cells to produce substance P, causing mast cell degranulation. Several studies have linked aeroallergen sensitization to chronic urticaria, and case reports recommend that allergen avoidance may be useful [6]. This study was conducted to investigate the clinical efficacy of allergen-specific immunotherapy in patients with CSU.

Methods

This Ex Post facto study was performed in the allergen immunotherapy clinic. Chest medicine department, Mansoura University. Patients diagnosed with CSU (with urticaria present at least 5 days a week) and receiving subcutaneous allergen-specific immunotherapy for at least 6 months duration were enrolled. Chronic spontaneous urticaria patients with intermittent remission and flare-ups course or who had known causes such as drugs or thyroid problems were excluded. This study was conducted within the requirements of the Mansoura University institutional research board (code number: R.23.02.2079). Demographic data, allergen sensitization patterns from skin prick test, urticaria

activity score, angioedema activity score, and medication scores were recorded. The scores recorded were measured before and after allergen immunotherapy. The skin prick test battery contained extracts of widespread aeroallergens in Egypt [7]. Extract used was prepared in the allergen immunotherapy preparation unit. Mansoura University [8] Pollen extract incorporated: (Chenopodium album, Conyza and tamarix aphylla pollen mixed in one bottle (pollen1)); (Polypogon monspeliensis, Cynodon dactylon and Arundo donax mixed in another bottle (pollen 2)).

The urticaria activity score evaluates two symptoms, the hives count and intensity of itching. The hives count was recorded from 0 to 3 where 0- no hives; 1 - less than 20 hives; 2 - 20-50 hives; 3 - >50 hives almost involved large confluent areas of wheals. The severity of itching was recorded as 0 - none; 1 - mild (present but not bothering or problematic); 2 - moderate (problematic but does not restrict the daily activity or sleep); and 3 - severe (interferes with normal daily activity or sleep) [9]. The following 5-point angioedema activity scale was used: 0 = absence, 1 = mild, 2 = moderate, 3 = severe, and 4 = very severe disease activity [10]. The medication score was assigned a value of zero for no medications, one for antihistamines, two for topical steroids, and 3 for systemic steroids [11]. The improvement level was calculated as follows: complete improvement; patients with lack of activity scores and stop medicines (both activity as well as medication scores = 0), partial improvement (regression in activity and/or medication scores but not attainment 0), and no improvement in both activity and medication scores.

Statistical analysis

Analysis of data was performed using SPSS v.16. Ordinal data were presented as numbers and

percentages. Continuous data was presented as mean and standard deviation. A comparison of paired ordinal data was accomplished utilizing Wilcoxon Signed Ranks Test. The association of allergen sensitization with improvement levels was established by Fisher's Exact test. The significance value was set at 0.05.

Results

This study included 32 patients with CSU (mean age 28 ± 14 years), 65.6% of them were females. 28.1% of them presented with CSU without angioedema. 65.6% of studied patients were sensitized to mixed pollen1 and 46.9% to mixed pollen 2. Both mold and mite sensitization were detected in 62.5 % of them. 81.2% and 78.1% of studied patients had a score of 3 for hives and itching scores respectively. However, 40.6% had a score of 4 for the angioedema table (1). There was a significant decline in activity and medication scores ($p < 0.0001$). 25% of studied patients had complete improvement in hives score and 15.6% in itching score. However, 43.5% and 42.9 % of them had complete improvement in the angioedema and medication scores respectively. 62.5%, 71.9 %, and 52.2% were partially improved in the hives, itching, and angioedema scores respectively. Also, 25% were partially improved in the medication score table (2,3). 2 patients had a recurrence of symptoms after initial improvement. One of them the recurrence occurred one year after immunotherapy and the other after 1.5 years. Pollens, mite, and mold sensitization were not associated with improvement in activity scores (hives score; p 0.2, 0.1, and 1 respectively. Itching score p 0.3, 0.2, and 1 respectively; angioedema score p 1,0.3 and 1 respectively) table (4).

Table 1: baseline data of included patients

	N (32)	%
Age: years (mean \pmSD)	28 \pm14	
Sex	11	34
Males' females	21	65.6
Skin prick test result*	20 /21 /15/6	62.5/65.6/46.9/18.8
Molds / MP1/MP2 / CD /feather/mite/hay	/ 8 /20/15	/25/ 62.5/46.9
Baseline hives score 1/ 2 /3	3/3/26	9.4/ 9.4 /81.2
Baseline itching score. 1/ 2 /3	3/4/25	9.4/ 12.5 /78.1
Baseline angioedema score. 0/1/ 2 /3	9/2/2/6/13	28.1/36.2/6.2/18.8/40.6
Baseline medication score 0 /1 /3	0/6/26	0 /18.7/81.3

*Not mutually exclusive, CD (cotton dust pollen), MP; mixed pollen

Table 2: Assessment of response to immunotherapy

	N (32) (%)	P value
hives score 0/1/ 2 /3	8/13/9/2 (25/ 40.6/28.1/6.2)	Z=-4.6* P <0.0001
itching score. 0/1/ 2 /3	5/13/12/2 (15.6/40.6/37.5/6.2)	Z=-4.5* P <0.0001
angioedema score. (n=23) 0/1/ 2 /3	10/7/6/0 (43.5/30.4/26.1)	Z=-4.1* P <0.0001
medication score. (n=28) 0 /1 /3	12/11/5 (42.9/39.3/17.9)	Z=-3.9* P <0.0001

Wilcoxon Signed Ranks Test

Table 3: improvement level after immunotherapy

	N (%)
Response (hives score)	
Complete improvement	8 (25)
Partial improvement	20 (62.5)
No improvement	4 (12.5)
Response (itching score)	
Complete improvement	5 (15.6)
Partial improvement	23 (71.9)
No improvement	4 (12.5)
Response (angioedema score) (n=23)	
Complete improvement	10 (43.5)
Partial improvement	12 (52.2)
No improvement	1(4.3)
Response (medication score) (n=28)	
Complete improvement	12 (42.9)
Partial improvement	7 (25)
No improvement	9 (32.1)

Table 4: association between allergen sensitization pattern and improvement

	Mite sensitization (n)	Significance
Hives score		X ² :3.5, p:0.1
improved	15	
not improved	5	
Itching score		X ² :2.7, p:0.2
improved	16	
not improved	4	
angioedema score		X ² :1.9, p:0.3
improved	15	
not improved	0	
	Pollen sensitization (n)	Significance
Hives score		X ² :2.3, p:0.2
improved	18	
not improved	5	
Itching score		X ² :1.7, p:0.3
improved	19	
not improved	4	
angioedema score		X ² :0.4, p:1
improved	15	
not improved	1	
	Mold sensitization (n)	Significance
Hives score		X ² :0.01, p:1
improved	17	
not improved	3	
Itching score		X ² :0.3, p:1
improved	17	

not improved	3	X ² :0.8, p:1
angioedema score		
improved	12	
not improved	1	

Discussion

CSU is mostly treated symptomatically. Numerous medications have been used, but none of them are curative. Antihistamines, anti-leukotrienes, corticosteroids, cyclosporin, hydroxychloroquine, dapsone, sulfasalazine, methotrexate, IV gamma globulin, and omalizumab are examples [12]. In the *Kasperska-Zajac* study [13], patients with a history of respiratory mite allergies and chronic urticaria had urticarial exacerbation after mite immunotherapy. This finding indicates that in some cases of chronic urticaria, dust mite allergens are causative or worsening variables that contribute to the development of the illness. In this study, 65.6% of studied patients were sensitized to mixed pollen 1 and 46.9% to mixed pollen 2. Also, Pollen sensitization is increased in patients with chronic urticaria in *Collins* study [14]. Urticaria in *Hesselmar et al* [15] was also significantly associated with sensitization to birch pollen. However, in our study sensitization pattern was not related to the level of improvement.

In this study, there was a significant decline in activity and medication scores after immunotherapy in patients with CSU. A higher percentage of them showed complete improvement in the angioedema and medication scores followed by the hives score. However, 2 patients had a recurrence of symptoms after initial improvement during the immunotherapy course. In accordance with our results, after one year of immunotherapy in the *Harfi* [16] study, most patients improved significantly, and most ceased symptomatic medication. Also, the Clinical efficacy of mite allergen immunotherapy has been proven to be good for urticaria patients in *Xing et al* [17]. *Kathuria et al* [18] hypothesize that combination therapy of omalizumab with house dust mite immunotherapy could provide increased clinical efficacy and quicker reaching of disease control in CSU.

Conclusion

immunotherapy is effective in patients with chronic spontaneous urticaria. No relationship was detected between sensitization patterns and symptom improvement.

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