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The Efficacy of Omalizumab Therapy in Chronic Inducible Urticaria

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ABSTRACT

Background: Immunoglobulin E antibody omalizumab is an effective and safe treatment option in patients with chronic urticaria and evidence is lacking in patients with chronic inducible urticaria (CindU). In this study, it was aimed to determine the efficacy of omalizumab in patients with CindU.

Materials and Methods: Patients treated with omalizumab resistant to second-generation antihistamine therapy were included in the study. Demographic characteristics, duration of disease, duration of omalizumab use and comorbidities of the patients were obtained from health records.

Results: We enrolled 27 patients ranging in age from 17 to 55 years, 9 patients had cholinergic, 2 aquagenic, 7 symptomatic dermographism, 4 cold, 4 pressure, 3 solar urticaria. Complete response was observed in 20 patients, partial response in 3 patients, and no response in 4 patients treated with omalizumab.

Conclusion: A higher percentage of patients had a complete response with 300 mg of omalizumab treatment.

Keywords: Urticaria, Inducible, Treatment

Introduction

Urticaria is a dermatologic disease which presents with recurrent wheals and/or angioedema. The disease seriously affects the quality of life of patients. Although there is no identified trigger associated with the appearance of signs and symptoms for chronic spontaneous urticaria (CSU), the appearance of symptoms in chronic inducible urticaria (CindU) is associated with a specific inducing factors. The types of CindU are physical (symptomatic dermographism, cold and heat urticaria, delayed pressure urticaria, solar urticaria, and vibratory angioedema) urticaria and non-physical urticaria (cholinergic urticaria, contact and aquagenic urticaria) [1,2].

Second-generation H1-antihistamines are the first-line treatment recommended for disease control in the treatment of CSU. Recent guidelines recommend increasing the dose up to four times when the standard dose is inadaquate to control symptoms [3]. Omalizumab, anti-Immunoglobulin E monoclonal antibody, is an effective and safe treatment option in patients with chronic urticaria who are resistant to antihistamine therapy. The efficacy of omalizumab in the treatment of CSU has been demonstrated in numerous randomized controlled trials and meta-analyses [4]. CindU often presents a major treatment challenge due to their resistance to first-line therapy with H1-antihistamines. Studies showing the efficacy of omalizumab in the treatment of CindU are limited [5]. In this study, we aimed to demonstrate the efficacy of omalizumab in CindU patients retrospectively.

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Materials and Methods

A total of 27 patients with CindU were treated with omalizumab in the dermatology department of Istanbul University Cerrahpasa-Cerrahpasa Faculty of Medicine between January 1, 2018 and May 31, 2021 (approval number: A-09, date:03.08.2021). Patients with CindU who were resistant to second-generation antihistamines and other conventional treatments were included in the study. We reviewed the health records of patients for demographic characteristics, duration of disease, duration of omalizumab use, and comorbidities. Disease severity was assessed using urticaria activity score; UAS7 score of ≤6 is well-controlled, 7-15 is mild, 16-27 modarate, 28-42 is severe urticaria. After omalizumab treatment, 50% or more improvement in UAS7 score was considered as complete response, less than 50% improvement as partial response, and those who did not show any change or showed an increase in disease severity were considered as non-responders. In addition, the efficacy of omalizumab treatment on the UAS7 score was evaluated by the change from baseline UAS7 to after UAS7 score. The ethical approvement was obtained from Istanbul University Cerrahpasa-Cerrahpasa Faculty of Medicine Institutional Review Board. Patients who denied research authorization were excluded. Omalizumab was used at a dose of 300 mg and repeated every month.

Statistical Analysis

Analyzes were performed by the use of the Statistical Package for the Social Sciences 2.0 version. The effiacy of treatment on symptom control was evaluated with the Wilcoxon test. A p-value of less than 0.05 was considered clinically significant.

Results

The mean age of 27 patients was 36.3 (17-55) and the mean disease duration was 4.8 years (Table 1). The types of CindU of parients included in the study were demonstrated in Table 2. There was no significant relationship between treatment response and disease onset severity, disease duration and age. It was observed that the duration of the disease was significantly higher in patients who received steroid therapy compared to those who did not receive steroid therapy (median duration 2 years and 3.75 years p=0.009). The mean duration of omalizumab use was 11 months. Before treatment, 20 patients had severe urticaria, 7 patients had moderate and 1 patient had mild urticaria. In 20 of 27 patients, complete treatment response was obtained. Three of 27 patients showed partial response while four patients showed no response to omalizumab treatment. Among non-responders, three patients had cholinergic urticaria and 1 had symptomatic dermographism. A significant difference was observed in baseline and post-treatment

Table 1. Demographic characteristics and features of patients

		n=27	%
Age*		36	17-55
Sex	Female	12	(44.4)
	Male	15	(55.6)
Disease duration (year)*		2	0.5-20
Type of inducible urticaria	Cholinergic	8	(29.6)
	Aquagenic	2	(7.4)
	Dermographism	7	(25.9)
	Cold	2	(7.4)
	Solar	2	(7.4)
	Pressure	4	(14.8)
	Cholinergic and cold	1	(3.7)
	Cold and solar	1	(3.7)
Duration of omalizumab use (month-dosage)*		8	2-39
Disease severity before treatment	Well controlled	0	(0)
	Mild	1	(3.7)
	Moderate	7	(25.9)
	Severe	19	(70.4)
Treatment response	No response	2	(7.4)
	Partial	10	(37.0)
	Complete	15	(55.6)

*n is the median values the % is the minimum and maximum values

UAS7 scores with omalizumab treatment (p<0.0001). The efficacy of omalizumab treatment on UAS7 score was shown in Table 2. No significant difference change was found between male and female patients in smyptom severity with omalizumab treatment (p=0.26). There was no significant difference in the change of disease severity in patients who used systemic steroids as previous treatment compared to patients who did not use systemic steroids (p=0.4) (Figure 1 and Table 3).

Discussion

In our study, omalizumab treatment was shown to be effective in patients with CindU. The efficacy of omalizumab in patients with cold urticaria, symptomatic dermographism and solar urticaria were demonstrated in placebo controlled randomized trials and phase 2 studies, respectively. The efficacy of omalizumab in pressure urticaria and cholinergic urticaria have been demonstrated in retrospective studies. Data showing the efficacy of omalizumab treatment on vibratory angioedema, aquagenic and contact urticaria were limited [6].

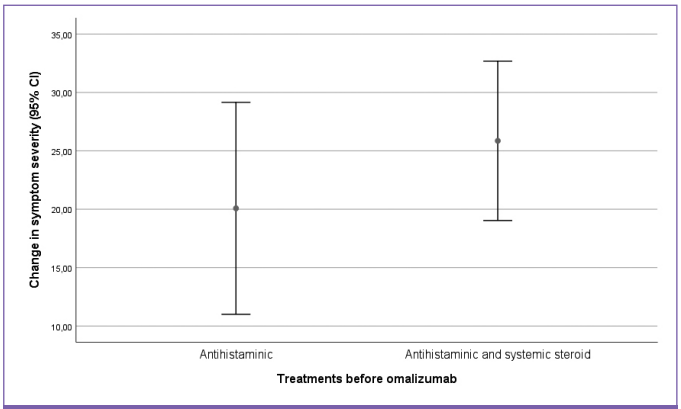

Figure 1. No significant difference in the change of disease severity in between previous treatments

Our study was showed that the duration of the disease was significantly higher in patients treated with steroids. The factors associated with longer disease duration; late-onset disease, relapsing course, concomitant CIndU, functional serum autoactivity, and insufficient response to a standard dose of antihistamine [7,8].

Symptomatic dermatographism is the most common type of physical urticaria, which presents as linear wheals in areas of friction or itching, such as collars and cuffs of clothes [9]. Our study showed a complete response in 6 of 7 patients with symptomatic dermographism. The efficacy of omalizumab in patients with symptomatic dermographism was demonstrated in a placebo-controlled randomized study involving 55 patients. Significant improvement in symptoms and dermatological quality of life index scores were observed with 150 and 300 mg omalizumab treatment compared to placebo after 10 weeks of treatment [10]. Metz et al. [11] showed complete response to omalizumab treatment in 86% of the patients with symptomatic dermatographism. In a another study, one of the two patients with symptomatic dermographism showed achieved complete/almost complete response to omalizumab treatment [12]. In a study of 25 patients treated with omalizumab, after 8 week treatment 3 patients with symptomatic dermographism had complete symptom control (defined as ≥90% improvement) [13].

Cold urticaria is itching, burning and wheals that develops within minutes in areas exposed to cold [14]. In our study, complete response was observed in 2 cold urticaria patients and partial response was observed in 2 patients with cold urticaria. In a placebo randomized controlled trial, the efficacy of 150 mg and 300 mg omalizumab were compared with placebo in 31 cold urticaria patients. After 4 weeks of treatment, significant improvement in symptoms was observed with omalizumab 150 mg and 300 mg compared to placebo and no significant difference was observed between these 2 doses of omalizumab [15]. In the case series of Kitsiolus et al. [16] in which 5 adolescent patients with cold urticaria were treated with

Table 2. The efficacy of omalizumab treatment on UAS7 score

		n	Mean score	Total score	z	p
UAS7 after - UAS7 baseline	Negative change	25[a]	13.92	348.00	-4.387	<0.0001
	Positive change	1[b]	3.00	3.00		
	Equal	1[c]				
	Total	27				

[a]UAS7 after<UAS7 baseline, [b]UAS7 after>UAS7 baseline, [c]UAS7 after=UAS7 baseline

Table 3. Relationship between previous treatments and changes in symptom severity with omalizumab treatment

	Change in symptom severity			p
	Percentile 25	Percentile 75	Median	
Antihistaminic	14.00	30.00	21.00	0.40
Antihistaminic and systemic steroid	21.00	35.00	25.50	

omalizumab 300 mg, a significant improvement in CDLQI score of 41.46% were reported in all patients after 5 months of treatment. Metz et al. [11] were reported complete response with omalizumab treatment in 3 of 6 cold urticaria patients. In a case series report, all 6 cold urticaria patients showed significant improvement in symptoms with omalizumab treatment [17].

Solar urticaria occur within minutes of exposure to ultraviolet or visible wavelengths of solar radiation [18]. In our study, complete response was obsorved with omalizumab treatment in 3 patients with solar urticaria. In a phase 2 multicenter study, the efficacy of omalizumab in solar urticaria was researched in 10 patients. At the end of 12 weeks of treatment with 300 mg omalizumab, 40% of patients achieved a DLQI score of less than 6 and 40% had a 50% improvement in severity of symptoms (measured on a visual analog scale) [19]. In a case series, significant improvement in symptoms was observed in 3 solar urticaria patients with omalizumab at varying doses of 150 mg to 450 mg [20].

Delayed pressure urticaria is characterized by the development of ıtchinng and wheals at sites of pressure to the skin [21]. In 3 of 4 delayed pressure urticaria patients, a complete response was obtained with omalizumab treatment in our study. The efficacy of omalizumab in delayed pressure urticaria was demonstrated in 2 retrospective studies. In the study of Ghazanfar et al. [12], 3 of 5 delayed pressure urticaria patients achieved a complete response with omalizumab treatment. In another study, complete response was observed in 7 of 8 pressure urticaria patients treated with omalizumab [11].

Study Limitations

The main limitations of our study are its retrospective nature and small sample size.

Conclusion

In conclusion, this retrospective analysis demonstrated the efficacy of omalizumab in different types of CindU. In addition, no relationship was found between omalizumab treatment and previous treatments in the change of disease severity to obtain more trustable results, there is need for more studies researching the efficacy of omalizumab in CindU.

Ethics

Ethics Committee Approval: The ethical approvement was obtained from Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine Institutional Review Board (approval number: A-09, date:03.08.2021).

Informed Consent: Retrospective study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ö.A., B.E., Concept: Ö.A., B.E., Design: Ö.A., B.E., Data Collection or Processing: S.B., Z.A.F., Analysis or Interpretation: Ö.A., Z.A.F., Literature Search: S.B., Z.A.F, Writing: S.B.

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