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Omalizumab: Anti-IgE Therapy in Severe Allergic Conditions

Arzu Didem Yalcin[1]* and Atil Bisgin[2]

[1]Department of Internal Medicine, Antalya Training and Research Hospital, Antalya, Turkey
[2]Department of Medical Genetics, Faculty of Medicine, Cukurova University, Adana, Turkey

Abstract

Background: The primary use of omalizumab (trade name Xolair) is for patients with severe, persistent and allergic asthma. Our aim was to evaluate the therapeutic efficacy of omalizumab as a treatment modality in patients with different allergic conditions.

Methods: There were eleven patients, whom followed-up with omalizumab therapy in the Immunology - Allergy Clinic, were evaluated by the clinical findings of nasal polyposis, anaphylaxis history, drug allergy, latex allergy, food allergy, autoimmune urticaria, allergic rhino-conjunctivitis, atopic dermatitis, angioedema and venom allergy.

Results: The patients, who had severe persistent asthma for periods ranging from 3 to 8 years, were enrolled in the study. Omalizumab was chosen as a potential new systemic therapy for the patients due to the clinical indication. Clinical symptoms of the all patients with severe persistent asthma were decreased. And in addition, asthma control test and pulmonary function tests were improved up. A severe anaphylactic reaction is prevented in a patient with 48 bee stings.

Conclusion: This clinical follow-up of omalizumab treated patients with severe persistent asthma and many different allergic conditions, suggests omalizumab is an effective therapy for asthma and different allergic conditions.

Keywords: Anti-IgE; Allergy; Rhinoconjunctivitis; Asthma; Co-morbid conditions

Introduction

The use of omalizumab has been evaluated in several allergic conditions, including allergic rhinitis, asthma, Churg-Strauss syndrome, atopic eczema, urticaria, angioedema, latex allergy, and concurrently with allergy immunotherapy to try to blunt reactions [1-10]. While approved by US Food and Drug Administration for asthma, the other indications need to be studied further. In this study, the omalizumab treatment efficacy was studied on severe persistent asthma patients with co-morbid allergic conditions.

The prevalence of respiratory symptoms, asthma, allergic rhino-conjunctivitis and respiratory function impairment among our Mediterranean region of Turkey; Antalya is considered to be higher than rest of the continent because of the climatic conditions [11]. So that omalizumab becomes more important to be used in stabilizing the clinical features of patients having more than one allergic condition.

Materials and Methods

Patients

Eleven patients were included in this follow-up study with severe persistent asthma whose mean age was 43 years and patient characteristics were given in table 1. They were all treated with omalizumab, had allergic rhinoconjunctivitis and all had a family history of atopia. All of the patients were followed-up in the Immunology-Allergy Clinics of Antalya Training and Research Hospital. The clinical findings of nasal polyposis, anaphylaxis history, drug allergy, latex allergy, food allergy, autoimmune urticaria, angioedema and venom allergy was evaluated.

Study design

The patients' written consent was obtained. All patients received omalizumab therapy for 24 months. Doses of omalizumab were administered every 2 weeks. Symptoms and severity of allergic reactions were recorded before and after being on omalizumab treatment. Assessments of clinical changes and adverse effects were made at every bimonthly patient visit. These assessments included vital signs, full physical examination, detailed possible allergy incidents, pulmonary function test and asthma control test (QualityMetric Inc.). Serum IgE levels, thyroid antibodies and eosinophil levels were evaluated in all patients.

Skin prick test (SPT)

SPTs were performed in all patients with standardized latex extract containing high ammonia natural rubber latex, with a battery of 35

Patient no.	Age (y)	Sex	Duration of severe persistent asthma	Total serum IgE (IU/mL)	Thyroid antibodies
1	61	M	8	424	Negative
2	38	M	4	446	(+) Antiperoxidase
3	47	F	6	273	Negative
4	41	F	6	488	Negative
5	18	F	4	542	Negative
6	56	F	4	135	Negative
7	49	M	3	348	Negative
8	33	F	5	249	Negative
9	18	M	4	317	Negative
10	61	M	3	485	Negative
11	51	F	4	650	Negative

Table 1: Patient characteristics.

***Corresponding author:** Arzu Didem Yalcin, Department of Internal Medicine, Allergy and Clinical Immunology Unit, Antalya Education and Research Hospital, Antalya, Turkey, E-mail: adidyal@yahoo.com

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P no.	Xolair Dose	Skin test sensitivity	SSTa	Allergic Reaction	Number of Injection	Efficacy of Omalizumab
1	375 mg q. 2 wk	Grass, tree, mold, mite	-	Aller rhin conj, AD	78	dose 3: AD and NSS improved significantly
2	225 mg q. 2 wk	Grass, mite, cockroach	+	Aller rhin conj, NP, MD Aller, angioedema and UC	72	dose 5: improvement in UC and angioedema attacks and NSS decreased
3	225 mg q. 2 wk	Grass, wheat, tree, mold, mite, cockroach, dog and cat epithelium	-	Aller rhin conj, NP	63	dose 3: improvement in NSS
4	300 mg q. 2 wk	Grass, wheat, tree, mold, mite, cockroach, honeybee, dog and cat epithelium	-	Aller rhin conj, NP venom aller, bee-sting anaphylaxis and UC	68	dose 1: decrease in NSS, dose 3: improvement in UC, dose 12: no anaphylactic reaction after 48 honey bee-sting.
5	300 mg q. 2 wk	mold, mite, cockroach, tomato, eggplant, strawberry, dog epithelium	-	Aller rhin conj, NP, food aller and anaphylaxis (food. induced)	64	dose 1: improvement in NSS dose 6: tolerated food allergy and no food induced UC
6	300 mg q. 2 wk	Grass, tree, mite, shrimp, perch, egg and latex	+	Aller rhin conj, NP, MD aller, food aller, latex aller, anaphylaxis (NSAID induced) and AD	72	dose 1: NSS decreased dose 5: AD and food allergy improved significantly dose 10: improvement in UC and angioedema attacks
7	300 mg q. 2 wk	wheat, tree, mite.	-	Aller rhin conj, NP, MD Aller and AD dermatitis	74	dose 3: improvement in NSS dose 5: improvement in UC
8	300 mg q. 2 wk	Grass, tree, mite, kiwi and orange	-	Aller rhin conj, NP, MD aller, food aller	76	dose 3: Improvement in UC attacks, NSS and F aller.
9	225 mg q. 2 wk	Grass, wheat, tree, mold, mite, cockroach, honeybee, dog and cat epithelium	-	Aller rhin conj, NP, MD Aller, venom aller and AD	72	dose 2: NSS improved dose 4: no exacerbation in AD
10	300mg q. 2 wk	Grass, mold, mite, cockroach	-	Aller rhin conj, MD aller, UC	64	dose 4: improvement in UC attacks, NSS
11	300mg q. 2 wk	Grass, tree, mite, dog epitelia	-	Aller rhin conj and AD	68	dose 2: NSS improves dose 6: no exacerbation in AD

AD: Atopic Dermatitis; Aller: Allergy; Conj: Conjunctivitis; MD: mMultidrug; NP: Nasal Polyp; NSAID: Non-Steroidal Anti-Inflammatory Drug; NSS: Nasal Symptom Scoring; P: Patient; Rhin: Rhinitis; SSTa: Autologous Serum Skin Test; UC: Urticarial

Table 2: Clinical follow-up criteria and changes with omalizumab.

common and 35 food allergens on the forearm. In additon, venom SPT was performed in 1 patient based on history. SPTs were performed by skilled nursing personnel. Positive tests were counted as wheals of 3 mm in diameter after 20 minutes. Tests were compared with positive histamine controls and negative saline controls. Commercial extracts used were manufactured by Alyostal ST-IR (Starallergenes S.A.-France). No intradermal testing was performed.

Autologous serum skin test

The test was performed by injecting 0.05 ml of the patient's own serum intradermally into the left flexor forearm, 2 inches below the antecubital crease and a saline control into the right forearm. A reading of the wheal was taken after 30 minutes. A wheal and flare of more than 1.5 mm diameter than that of the control was considered positive.

Results

In this clinical follow-up study, 11 patients were on omalizumab treatment and they were all clinically analyzed at our clinic. The patients had severe persistent asthma for periods ranging from 3 to 8 years. All patients maintained significant improvement by history as shown by a decrease in clinical symptoms and increase in asthma control test. The allergic symptoms were improved clinically and summarized in table 2 and the changes in steroid usage were in table 3.

The Asthma Control Test (ACT) and an Asthma Control Questionnaire were completed by all patients at three clinical visits at the beginning of the omalizumab treatment and 48 to 56 weeks apart. Pulmonary function was also measured. All of the patients had an ACT score of <20, indicating that asthma was not well controlled on previous treatment, before the omalizumab therapy. As shown in figure 1, after the treatment period of 12 to 24 months of omalizumab, the ACT score increased up to 20-24 which was indicated as "well-controlled" asthma.

Discussion and Conclusions

Omalizumab was developed for the treatment of severe allergic asthma. It blocks binding of free IgE on basophils and mast cells, thus inhibiting their activation by allergens. Omalizumab treatment significantly reduces the nasal and conjunctival symptom scores of all patients. This demonstrates the effectiveness of omalizumab and these findings agree with recently published data [12,13].

In this follow-up, omalizumab significantly improved asthma control and pulmonary function in patients with severe persistent asthma. Patients no 1, 2 and 4 did not show an increase of ACT up to 20. Although, they showed no asthma exacerbation after the treatment, there was a 2.5 fold increase in ACT scoring.

Seven of the patients' had chronic urticaria, while 2 of them with chronic autoimmune urticaria. There is a significant improvement in urticaria attacks beginning from the 3rd dose in all of these patients. However, the patients with autoimmune urticaria had been under treatment for longer period before the symptoms were decreased. Similar results were also reported in previous study about the omalizumab effectivity in the treatment of chronic autoimmune urticaria [9,14].

Patient no 5, 6 and 8 had a history of food allergy. While treating asthma patients with omalizumab, patients subjectively observed a reduction in their concomitant food allergy symptoms as previously reported [8,15].

There is a history of honey-sting allergy in patients no 4 and 9. The patient no 4 had previously reported honeybee induced anaphylaxis. Interestingly in this patient, while having the omalizumab treatment

Patient no.	Pre-omalizumab oral steroid dose (mg/day)	Post-omalizumab
1	6	0
2	8	0
3	0	0
4	12	0
5	0	0
6	6	0
7	0	0
8	6	0
9	0	0
10	10	0
11	8	0

Table 3: Steroid doses of the patients pre- and post-omalizumab.

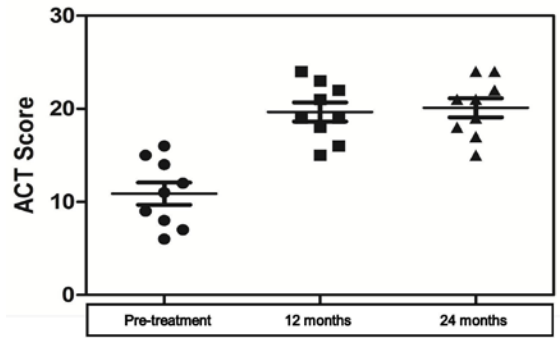

Figure 1: Asthma control test.

on the 12th dose, she had 48 bee-stings and developed only a slight local reaction which resolved spontaneously. The results were in concordance with similar cases that were treated with omalizumab in the literature [16,17]. Allergen immunotherapy has been used in the management of allergic diseases for nearly 100 years [18]. It is the only specific treatment for hymenoptera venom anaphylaxis [19-21]. Various venom immunotherapy schedules have been designed to treat anaphylaxis [22-27]. Though the effect of venom immunotherapy is well documented, there is also an increased risk of side-effects that were in a large range from itchy eyes, sneezing to Jessner lymphocytic infiltrate and severe anaphylaxis in bee-venom-treated patients and in those with rapid dose increase [28-30]. This case suggests that omalizumab may be able to prevent severe anaphylaxis during immunotherapy.

Latex allergy is another important health problem since 1980s. Latex sensitivity was found as 18.1% in our previous study [31]. The patient no 6 had a history of latex allergy; the improvement in this allergy persists after the 5th dose of omalizumab similar to previously reported in the literature [32].

The most recent studies on severe persistent allergic asthma and the effect of omalizumab treatment, provided novel perspectives on using serum soluble TNF-related apoptosis inducing ligand, nitric oxide, malondialdehyde, hydrogen peroxide and albumin levels, total antioxidant capacity and ceruloplasmin activity as an efficacy marker [33-36].

As a conclusion, our clinical follow-up of omalizumab treated patients with severe persistent asthma suggests that omalizumab is an effective therapy for asthma and as well as for several allergic conditions.

Authors Contributions

Clinical follow-up: Arzu Didem Yalcin analyzed the data; Atil Bisgin wrote the paper; Arzu Didem Yalcin and Atil Bisgin drafted the figures. All authors read and approved the final manuscript.

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