İstanbul Med J 2017; 18: 135-8
DOI: 10.5152/imj.2017.93653

Original Investigation

Omalizumab Treatment in Patients with Severe Allergic Asthma

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Abstract

Introduction: Omalizumab is a monoclonal antibody used for treating patients with severe allergic asthma. It has has been shown to be effective and is being increasingly used. This study aimed to evaluate the long-term efficacy and safety of omalizumab treatment in patients with severe allergic asthma.

Methods: The efficacy and safety of omalizumab treatment was assessed by analyzing the medical records of the patients. While patients were on omalizumab treatment, they were clinically evaluated monthly. The level of control of asthma symptoms as determined in the Global Initiative for Asthma (GINA) guideline was used to evaluate the efficacy of treatment.

Results: Fifty-four patients were included. All patients were sensitive to at least one perennial allergen and had uncontrolled allergic asthma despite providing standard treatments. The mean±standard deviation (SD) age, body weight, and IgE level were 53.6±13.9 years, 75.4±14.3 kg, and 294.7±227.5 IU/mL, respectively. The mean±SD omalizumab treatment duration was 34.8±20.2 (range,10-84) months. Patients did not experience major adverse reactions that were considered related to omalizumab treatment. Two patients had local adverse reactions, and one had myalgia that was considered to be drug-related. After omalizumab treatment, asthma symptoms were well controlled in 25 patients (46.3%), partly controlled in 23 patients (42.6%), and uncontrolled in 6 patients (11.1%).

Conclusion: Our study showed that omalizumab treatment is well tolerated and effective for patients with uncontrolled allergic asthma.

Keywords: Asthma, omalizumab, severe allergic asthma, uncontrolled allergic asthma

Introduction

Asthma affects an estimated 300 million individuals worldwide, but it can be seen in patients of all age groups and is an important global health problem that is increasingly prevalent in many developing countries. Thus, the treatment cost of asthma is rising and it is an increasing burden on patients and the society (1).

Omalizumab reduces the free immunoglobulin E (IgE) level in the blood by binding to serum-free IgE. In addition, the effector cells inhibit the binding of IgE to high affinity receptors on the surface without causing degranulation of susceptible cells; therefore, a recombinant human monoclonal antibody inhibits the effector functions of IgE. Eventually, omalizumab prevents the effector cell degranulation induced by sensitive allergen and reduces the early and late phase responses to inhaler allergens (2).

Allergic and IgE-mediated mechanisms play a role in a significant proportion of asthmatic patients with uncontrolled asthma. The anti-IgE therapy is a recombinant human monoclonal antibody, which is used in patients with moderate or severe allergic asthma not controlled by omalizumab and whose efficacy and safety have been proven (3-8).

In the Global Initiative for Asthma (GINA) guidelines, an increase in the "step-up" therapy is recommended until asthma control is achieved. In patients with asthma who are not adequately controlled by long-acting beta agonist (LABA), leukotriene receptor antagonist (LTRA), or theophylline in combination with a medium- or high-dose inhaled corticosteroid (ICS), GINA recommends to add a tiotropium inhaler for patients with over 12 frequent exacerbations, omalizumab for those with severe allergic asthma, and mepolizumab (anti-interleukin [IL] 5) for those with severe eosinophilic asthma at stage 5 of treatment (9).

In our country, omalizumab can be prescribed for the patients aged ≥12 years; weighing 20–150 kg; having severe persistent allergic asthma; not responding to the treatment despite high-dose

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Received: 06.10.2016

Accepted: 08.02.2017

ICS and LABA and/or LTRA therapy; who have been proven sensitive to at least one perennial allergen (eg, house dust mites, cat and dog hair, cockroaches, and mold spores; through skin tests or specific IgE positivity); and having a serum IgE level determined as 30–1500 IU/mL.

Many review articles and meta-analyses have shown that omalizumab treatment does not increase the incidence of a common side effect (10, 11).

After the omalizumab therapy was approved for the use in appropriate patient groups, it was also implemented in our hospital in accordance with the indications determined by the Ministry of Health. The aim in this study was to evaluate the safety and efficacy of omalizumab treatment. Here we report our experience of real-world omalizumab treatment in allergic asthmatic patients with uncontrolled IgE levels between 30–1500 IU/mL and with sensitivity to at least one perennial allergen.

Methods

The records of 8530 patients with asthma followed up in our clinic since 2010 were retrospectively reviewed. Of the 61 patients with severe persistent allergic asthma in whom omalizumab (Xolair; Novartis, Basel, Switzerland) treatment was applied, 54 patients who continued the treatment at the end of the 16 weeks were included in the study (Figure 1).

The patients were diagnosed and treated in accordance with the GINA guidelines. Omalizumab treatment was administered according to the criteria of Ministry of Health. All patients had been treated with high-dose ICS, LABA, and LTRA before starting omalizumab therapy. Despite the combination treatment, omalizumab was started for adult patients who weighed 20–150 kg and had severe persistent allergic asthma with symptoms that could not be controlled, who were proven sensitive to at least one perennial allergen (eg, house dust mites, cat and dog hair, cockroaches, and mold spores; through skin tests or specific IgE positivity), and who had serum IgE levels of 30–1500 IU/mL.

The dose was administered through subcutaneous injection every 2 or 4 weeks as indicated in the omalizumab dose schedule, according to the body weight of the patient and the total IgE levels at the start of treatment. All patients were kept under observation for 2 hours after the first three injections and 1 hour after the subsequent injections for noting any side effects of the medication. In addition, before treatment, the patients were trained on the possibility of delayed reaction and informed about the anaphylactic symptoms and signs.

The patients were evaluated monthly in terms of side effects and efficacy. The treatment efficacy was classified as well controlled, partially controlled, and uncontrolled, which is based on the asthma symptom control level according to the GINA assessment of asthma control in adults (9). Spirometry was administered at the beginning of the treatment and every 3 months.

The approval for this study was obtained from the Ethics Committee of Antalya Training and Research Hospital. Informed consent was not obtained from the patients because the file records of patients were examined retrospectively after the ethics committee's approval.

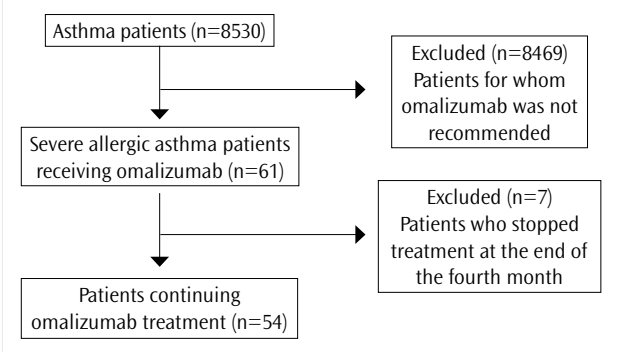

Figure 1. Follow-up chart of the patients with asthma

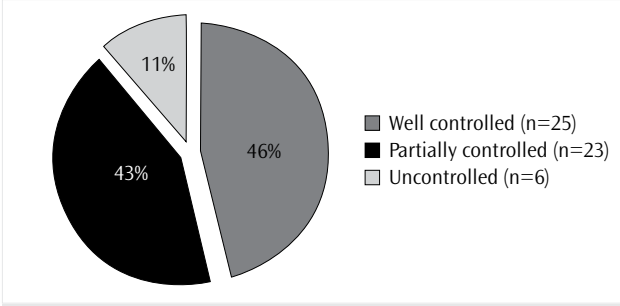

Figure 2. The level of asthma symptom control in patients after omalizumab treatment

Statistical analysis

Descriptive statistics used in the study were indicated as mean±standard deviation (SD), number (n), and percentage.

Results

The demographic and clinical characteristics of the included patients are shown in Table 1. Fifty-four patients who had been recommended omalizumab for allergic asthma since 2010 and who were continuing the treatment at the end of the 16 weeks were included in the study. The mean age of the patients (years±SD) was 53.6±13.9 (min-max: 21–87 years), and the mean duration of omalizumab use (month±SD) was 34.8±20.2 (min-max: 10–84 months). While the mean serum IgE level (IU/mL±SD) was 294.7±227.5 (min-max: 32–1179 IU/mL) and 46 (85.2%) patients had house dust mite sensitization, 13 patients (24.1%) had mold and epithelium sensitization, 11 patients (20.4%) had grass pollen sensitization, and 4 patients (7.4%) had olive pollen sensitization. Forty-five (83.3%) patients had never smoked, 6 of them (11.1%) quit smoking, and 6 (11.1%) were still smoking. Four patients (7.4%) had chronic obstructive pulmonary disease (COPD) in addition to asthma.

In the last evaluation of patients after omalizumab treatment, the asthma symptom control level in 48 (88.9%) patients was better than that at the start of treatment. Asthma symptom control level was well controlled in 25 (46.3%) patients, partially controlled in 23 (42.6%) patients, and uncontrolled in 6 (11.1%) patients (Figure 2).

Only two patients were noted with a local reaction at the injection site during the examination of the side effects recorded in the course of treatment. In one patient, myalgia was detected. A 77-year-old patient died of bronchial carcinoma. There was no sys-

Table 1. Clinical and demographic characteristics of 54 patients at the start of treatment

Characteristics	Findings
Age (mean±SD) (years)	5.6±13.9
Female (n) (%)	38 (%70.4)
Total IgE (mean±SD) (IU/mL)	294.7±227.5
Body weight (mean±SD) (kg)	75.4±14.3
FEV1 (L) (%) (mean±SD)	1.68±0.65 (%61.6±16.5)
Skin test positivity (n) (%)	
House dust mites	46 (85.2)
Mold	13 (24.1)
Grass pollen	11 (20.4)
Epithelium	13 (24.1)
Olive	4 (7.4)
Smoking (n) (%)	
Non-smoker	42 (77.8)
Ex-smoker	6 (11.1)
Smoker	6 (11.1)

IgE: immunoglobulin E; FEV1: forced expiratory volume in the 1 second; SD: standard deviation

temic side effect thought to be related to the drug. There were no problems in the clinical evaluation and physical examination in patient follow-ups. Omalizumab treatment was found to be well tolerated.

Discussion

Here, we presented the real-world data on drug efficacy and side effects in a group of patients who were followed up for severe allergic asthma and administered omalizumab. This study showed that long-term omalizumab administration was well tolerated in our patients, and it was safe and effective. In earlier studies and reviews, omalizumab treatment has proven to be effective and safe in severe allergic asthmatic cases (10-12). However, there were few studies on this subject in Turkey (13, 14). In a real-world study conducted by Bavbek et al (13), the evaluations of 18 patients 1 year before treatment were compared with their conditions when they were included into the study. While the systemic steroid dose decreased at a rate of 83%; the number of other asthma medications at a rate of 28%; and the number of attacks, emergency service applications, and hospitalizations at the rate of 93%, 95%, and 86%, respectively, there was no difference in the forced expiratory volume in 1 second (FEV1) values. However, the asthma control test scores of the patients were found to increase at a rate of 94% with omalizumab treatment. In a study by Özgür et al (14), in 26 asthmatic patients treated with omalizumab, the duration of omalizumab treatment was 40.81±8.2 months and an improvement was also detected in FEV1 and in asthma control test scores of all patients compared to the baseline values. In addition, there was a significant decrease ($p<0.05$) in the number of attacks of the patients, emergency service applications, and the use of systemic glucocorticoids and short-acting beta2-agonists at the end of 36 months; the life quality of patients was also improved.

In our study, 54 patients were administered omalizumab due to severe allergic asthma, and the duration of treatment (months±SD) was 34.8±20.2 (min-max: 10–84 months). A literature review, which analyzed seven randomized clinical trials and 18 real-world data on omalizumab treatment in severe allergic asthma, showed that the duration of follow-ups was longer in studies reflecting the daily clinical practice better and real-life data than randomized clinical trials (18.29 vs 8.57 months) (12). From this point of view, the mean omalizumab treatment duration was 34.8±20.2 months in our study, which was relatively good compared to other studies.

In terms of efficacy, our findings were consistent with literature (10-14). While only 11.1% of our patients did not benefit from the treatment, 88.9% were benefited. In a review of real-world activity studies conducted in 32 countries with 4117 patients who had severe allergic asthma and were treated with omalizumab, it was shown that omalizumab therapy was associated with significant improvements against the objective and subjective load of the disease chain of severe allergic asthma (15). Four of our patients had COPD as well as asthma, and they were referred as the patients having Asthma-COPD overlap syndrome (ACOS) according to the latest guide (16). The efficacy of omalizumab treatment was demonstrated in a recently published series of an ACOS group (17).

Considering the side effects, muscle pain that was thought to be drug-related was seen in a patient, but no problems were noted in the follow-up and physical examination of this patient. In two patients, local edema and hyperemia were seen as side effects at the injection site. No major side effects, such as anaphylaxis, associated with omalizumab were observed. Omalizumab therapy was well tolerated. However, a 78-year-old patient who had been receiving omalizumab for 40 months and had never smoked died of lung cancer. This condition was not associated with omalizumab. Cancer risk increase with omalizumab has not been reported in literature. In an epidemiological study conducted on omalizumab, while the malignancy rate in cohorts receiving and not receiving omalizumab was 0.84 (95% confidence interval [CI], 0.62–1.13) for all malignancies, it was 0.98 (95% CI, 0.71–1.36) when non-melanoma skin cancers were excluded (18). In another randomized, double-blind, placebo-controlled clinical trial performed by Busse et al. (19), no relationship was detected between omalizumab treatment and malignancy risk. It has been shown in many reviews, meta-analyses, and studies that omalizumab therapy does not affect the overall incidence of side effects (10, 11). In an analysis of an 8-placebo-controlled study published by Rodrigo et al. (20), while the incidence of serious adverse events was 5.3% in the placebo group, it was 3.8% in the group receiving omalizumab ($p=0.14$); a hypersensitivity reaction was reported as an anaphylactic reaction in two cases in the patient group receiving omalizumab and in one case in the placebo group, but there was no statistically significant difference between the groups.

The strength of our study was that the duration of omalizumab treatment was significantly long (34.8±20.2 months). Besides, we think that the retrospective analyses also convey real-world experiences and that they are valuable since the patient population is heterogeneous. The limitations were that it was a single-centered study with a small sample size.

Conclusion

In patients administered omalizumab and followed due to severe allergic asthma in our center, omalizumab treatment was shown to be effective in the real-world conditions and safe in terms of side effects.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Antalya Training and Research Hospital.

Informed Consent: Informed consent was not received because the study was made retrospectively by examining file records of the patients after ethic committee approval.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - T.S.T., A.Ç.; Design - T.S.T., A.Ç.; Supervision - T.S.T., A.Ç.; Resource - T.S.T., A.Ç.; Materials - T.S.T., A.Ç.; Data Collection and/or Processing - T.S.T., A.Ç.; Analysis and/or Interpretation - T.S.T., A.Ç.; Literature Search - T.S.T., A.Ç.; Writing - T.S.T., A.Ç.; Critical Reviews - T.S.T., A.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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Cite this article as: Tat TS, Çilli A. Omalizumab treatment ın patients with severe allergic asthma. İstanbul Med J 2017; 18: 135-8.