Orginal Article

Is Omalizumab Alone an Effective Treatment for Patients with Chronic Spontaneous Urticaria?

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Abstract

Aim: While 2nd generation antihistamines are the first-line treatment for chronic urticaria (CU), omalizumab is recommended for the treatment of patients with inadequate response to these drugs. This study investigated the need for additional treatment while using omalizumab and the factors affecting this need.

Materials and Methods: In this study, we retrospectively evaluated the patients who were admitted to our dermatology clinic who started and continued to receive omalizumab at the recommended standard dose between January 01, 2023 and May 01, 2023 for CU.

Results: Among 90 patients with chronic spontaneous urticaria receiving omalizumab, 51 (56.7%) needed additional treatment, whereas 39 (43.3%) did not need any additional treatment. However, of the 51 patients who developed complaints, 42 (82.4%) had their complaints controlled with antihistamines only, 7 (13.7%) with antihistamines and systemic steroids, 1 (2%) with systemic steroids only, and 1 (2%) with antihistamines, chloroquine, and cyclosporine. Among the patients who used antihistamines to control their complaints, the minimum antihistamine dose was once a day in 33 patients (66%), 2 times a day in 13 patients, 3 times a day in 3 patients and four times in 1 patient.

Conclusion: A considerable number of patients with CU using omalizumab did not need additional treatment, and the complaints of patients who needed additional treatment were managed with low-dose antihistamines in a short period.

Keywords: Chronic urticaria, omalizumab, antihistamine

Introduction

Omalizumab is a DNA-derived, recombinant humanized immunoglobulin G1κ (IgG1κ) monoclonal antibody that selectively binds to human IgE.[1] It downregulates the receptor and suppresses the secretion of inflammatory mediators by reducing the IgE response to allergic response by 95%.[2] This is the first pharmaceutical to be approved for use in patients with chronic idiopathic urticaria/chronic spontaneous urticaria (CSU) who have not responded to treatment with an H1 antihistamine.[3-5] The approval of omalizumab by health authorities in many countries and its use in clinical practice has provided significant progress in the treatment of patients with chronic urticaria (CU), but there are still groups of patients whose symptoms cannot be controlled with existing treatments and who need other options.[4,6]

Objectives

Omalizumab is recommended in the current guidelines to be used in addition to antihistamines in patients with refractory CSU.[7] Nevertheless, there is evidence that it is effective when used alone in some patient groups.[8,9] The objective of this study was to investigate the necessity for supplementary treatment

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and the factors influencing this requirement in patients with CU who are undergoing treatment with omalizumab at the recommended dosage.

Materials and Methods

In this study, patients who were admitted to Dicle University Faculty of Medicine, Department of Dermatology and started and continued to use omalizumab at the recommended dose between January 01, 2023 and May 01, 2023 due to CSU were retrospectively included. This study was approved by Dicle University Non-Interventional Clinical Research Ethics Committee (approval number: 219, date: 17.05.2023).

Patients were evaluated in terms of age, gender, occupation, educational status, height, weight, smoking history, duration of disease, duration of omalizumab use, history of systemic disease, need for additional treatment while using omalizumab until the next dose, if additional treatment was needed, with which group of drugs the symptoms were controlled, the dose and duration of use of the drug that controlled the symptoms, and the time it took for the symptoms to recur when the drug that controlled the symptoms was stopped. Patients with CSU lasting longer than 8 weeks who had used at least one approved antihistamine and who were followed up at our center were included in the study. The exclusion criteria were physical urticaria and weight 20 kg.

Statistical analysis

IBM SPSS 21.0 for windows statistical package was used for the statistical evaluation of the research data. Measurable variables were presented as mean ± standard deviation, and categorical variables were presented as number and percentage (%). We checked whether the data fit the normal distribution. The hypotheses were taken as two-way, and $P \leq 0.05$ was accepted as indicating statistical significance.

Results

A total of 90 patients were included in the study, of which 57 (63.3%) were female and 33 (36.7%) were male. The ages of the patients ranged from 10 to 73 years, with a mean age of 39.08±12.94 years. The average age of male patients was (40.18±14.32) and the average age of female patients was (38.45±12.15).

It was determined that 39 (43.3%) of the patients included in the study did not need any additional treatment during omalizumab therapy (Table 1).

Of the patients included in the study, 41 (45.6%) had chronic urticaria for more than 5 years, 39 (43.3%) for 1-5 years, and 10 (11.1%) for less than 1 year. Forty-seven (52.2%) patients had been on omalizumab for 6 months-1 year, 31 (34.4%) for less than 6 months, and 12 (13.3%) for more than 1 year.

When the duration of omalizumab use was compared according to patient sex, it was observed that the duration of omalizumab use in men and women was similar, and there was no significant difference between the groups ($P > 0.05$). There was a weak positive correlation ($r = 0.353$; $P < 0.05$) between the duration of chronic urticaria and the duration of omalizumab use.

The incidence of developing adverse effects before the administration of the subsequent dose of omalizumab was markedly higher in female patients enrolled in the study (64.9%) than in male patients (42.4%) ($P < 0.05$) (Table 2).

In the analysis performed to determine whether there was a relationshipbetween the duration of CU and the development of complaints until the time of administration of the other dose while using omalizumab, the rate of development of complaints until the time of administration of the other dose while using omalizumab was found to be 70% in patients with a CU duration of less than 1 year, 61.5% in patients with a duration of 1-5 years, and 48.8% in patients with a duration of more than 5 years, but there was no significant relationship ($P > 0.05$).

While using omalizumab, 51 of the patients included in the study developed complaints up to the time of administration of the next dose, of which 18 (35.3%) developed complaints at 4th week after the last dose, 14 (27.5%) at 3rd week, 10 (19.6%) at 2nd week, 6 (11.8%) at 1st week, and 3 (5.9%) at any time.

In the one-way analysis of variance performed to determine whether there was a difference in terms of mean age between patients who developed complaints and those who did not develop complaints until the time of administration of the other dose while using omalizumab, the mean age was found

Table 1. Distribution of patients according to the development of complaints during omalizumab therapy

Complaint	n, (%)
Yes	51 (56.7)
No	39 (43.3)
Total	90 (100)

Table 2. Comparison of the development of complaints while using omalizumab until the time of administration of the next dose according to patient gender

		Gender				
Complaint		Female	Male	Total	χ^2	p-value
Yes	n (%)	37 (64.9)	14 (42.4)	51 (56.7)		
No	n (%)	20 (35.1)	19 (57.6)	39 (43.3)	4.304	0.038
Total	n (%)	57 (100)	33 (100)	90 (100)		

Table 3. Distribution of patients according to the drug group they benefited from upon complaint

Drugs	n	(%)
Antihistamine	42	82.4
Systemic steroids	1	2.0
Antihistamine and systemic steroid use	7	13.4
Antihistamines, chloroquine, and cyclosporine	1	2.0
Total	51	100

to be higher in patients who developed complaints, but the difference between the groups in terms of mean age was not significant ($P > 0.05$).

In the calculation performed to determine whether there was a relationship between the duration of omalizumab use and the week of onset of complaints until the time of administration of the next dose while using omalizumab, a significant relationship was found between the duration of omalizumab use and the week of onset of complaints ($P < 0.05$). The results of the statistical analysis showed that complaints started in the 1st week in 35.3% of patients who had been using omalizumab for less than 6 months, in the 3rd week in 34.5% of those who had been using it for 6 months-1 year, and in the 3rd week in 40% of those who had been using it for more than 1 year.

Table 3 presents the drugs that patients benefited from when their complaint was initiated. Accordingly, 42 (82.4%) of the 51 patients with complaints benefited from antihistamine, 7 (13.7%) benefited from antihistamine and systemic steroid, 1 (2%) benefited from systemic steroid only, and 1 (2%) benefited from antihistamine, chloroquine, and cyclosporine.

When the drugs used by the patients who controlled their complaints with antihistamines were analyzed, 17 (34%) of the patients used bilastine, 13 (26%) levocetirizine, 7 (14%) cetirizine, 6 (12%) desloratadine, 3 (6%) ebastine, 2 (4%) loratadine, and one patient (2%) each used fexofenadine and bilastine + rupatadine.

The minimum antihistamine dose that controlled the complaints was once aday in 33 patients (66%), twice a day in 13, 3 times a day in 3, and four times a day in 1.

Twenty-three patients (46%) used antihistamines for 1 week, 19 (38%) for 2 weeks, 7 (14%) for 4 weeks, and 1 (2%) for 3 weeks until the next omalizumab dose.

It was observed that the use of methylprednisolone controlled the complaints in 8 of the patients included in the study, and the minimum dose of methylprednisolone that controlled the complaints was 36 mg in 4 (50%) of these patients, 16 mg in 3 (37.5%), and 48 mg in 1 (12.5%). Among the 8 patients who received methylprednisolone, 4 (50%) received it for 2 weeks, 3 (37.5%) for 1 week and 1 (12.5%) for 4 weeks. The body mass index (BMI) of the patients ranged from 17.10 to 29.30 kg/m^2, and the mean BMI was calculated as 23.31±2.64 kg/m^2. Although the mean BMI of women (23.51±2.63 kg/m^2) was found to be higher than that of men (22.95±2.67 kg/m^2), there was no significant difference between both genders in terms of BMI ($P > 0.05$). There was a significant correlation between the BMI of the patients included in the study and the duration of chronic urticaria disease ($P < 0.05$).

Discussion

According to the 2022 international EAACI/GA^{2}LEN/EuroGuiDerm/APAAACI guidelines in 2022, the use of standard doses of 2nd generation H1 antihistamines is recommended as the first-line symptomatic treatment for CSU. If needed, the dose can be increased up to four times. If symptoms do not improve, omalizumab (300 mg) should be added to the treatment within 2-4 weeks. If necessary, the dose can be increased and the intervals shortened. If symptoms do not resolve, cyclosporine up to 5 mg/kg can be added to treatment in addition to a second-generation antihistamine at 6 months or sooner. Short-term glucocorticoids may be considered in severe exacerbations.[7]

Although antihistamines remain the mainstay of urticaria treatment, some patients may not require antihistamines once the disease is controlled with omalizumab.[8]

Of the 90 patients included in this study, 39 (43.3%) did not require additional treatment. In contrast, 51 patients (56.7%) developed complaints during omalizumab therapy and required additional treatment. Melé-Ninot et al.[8] included 298 patients with CSU and reported that 23.5% of the patients stopped taking antihistamines during omalizumab treatment. However, Ensina et al.[9] reported that 17 out of 53 patients (32.1%) who used omalizumab and were treated for 24 months continued treatment without antihistamines.

In our study, the minimum dose of antihistamine that controlled the complaints was once a day in 33 (66%) of the patients who used antihistamines to control their complaints, 2 times a day in 13, 3 times a day in 3, and 4 times a day in 1. Among our patients who needed antihistamines, 23 (46%) used antihistamines for 1 week, 19 (38%) for 2 weeks, 7 (14%) for 4 weeks, and 1 (2%) for 3 weeks until the next omalizumab dose. Although no study has been conducted to support this finding, it was observed that most patients who needed additional treatment relieved their complaints with low doses, such as a single dose per day.

A weak, positive correlation (r=0.353; $P < 0.05$) was found between the duration of chronic urticaria and the duration

of omalizumab use. Ghazanfar et al.[10] reported a positive correlation between the duration of disease and the duration of omalizumab use in their study. Similarly, Vadasz et al.[11] reported a positive correlation between the duration of disease and the duration of omalizumab use. It can be seen that the results obtained from our study are compatible with the literature.

Female patients had a significantly higher rate of complaint (64.9%) than male patients (42.4%) when using omalizumab until the next dose. No study on this result was found in the literature.

The mean age was found to be higher in patients who developed complaints until the duration of treatment while using omalizumab, the difference between the groups in terms of mean age was not significant.

In a study by Maurer et al.[12], the average age of patients who developed complaints while using omalizumab was higher.

In the analysis performed to determine whether there was a relationship between the duration of CU and the development of complaints until the time of administration of the other dose while using omalizumab, the rate of development of complaints until the time of administration of the other dose while using omalizumab was found to be 70% in patients with a CU disease duration of less than 1 year, 61.5% in patients with a duration of 1-5 years, and 48.8% in patients with a duration of more than 5 years, but there was no significant relationship. No study on this result was found in the literature. The results demonstrated that as the duration of chronic urticaria increases, the rate of complaint development decreases until the next dose of omalizumab administered.

The mean ages of patients who developed complaints and those who did not develop complaints until the time of administration of the next dose while using omalizumab were similar. Maurer et al.[12] reported a relationship between age and complaint development and that the rate of complaint development increased with increasing age while using omalizumab.

As a result of the chi-square analysis performed to determine whether there was a relationship between the duration of omalizumab use and the week of onset of complaints until the time of administration of the next dose while using omalizumab, a significant relationship was found between the duration of omalizumab use and the week of onset of complaints ($P < 0.05$). As a result of the statistical analysis, 35.3% of patients who had been using omalizumab for less than 6 months started to complain in the 1st week, 34.5% of those who had been using it for 6 months-1 year started to complain in the 3rd week, and 40% of those who had been using it for more than 1 year started to complain in the 3rd week. Thus, as the duration of omalizumab use increases in patients with chronic urticaria, the week of onset of complaints until the administration of the next dose is postponed.

Of the 51 patients who developed complaints while using omalizumab, 42 (82.4%) benefited from antihistamines, 7 (13.7%) from antihistamines and systemic steroids, 1 (2%) from systemic steroids, and 1 (2%) from antihistamines, chloroquine, and cyclosporine. Forty-five (88.2%) patients who developed complaints stated that their complaints resumed when they stopped taking antihistamines for 1-5 days and 6 (11.8%) patients stated that their complaints resumed when they stopped taking antihistamines for 6-10 days.

There was a correlation between BMI and duration of chronic urticaria disease. The duration of chronic urticaria disease was longer in patients with higher BMI. Zbiciak-Nylec et al.[13] reported that obesity was an important risk factor for urticaria. The findings of our study are consistent with those reported in the existing literature on this topic.

Conclusion

Guidelines recommend the addition of omalizumab to the treatment of patients with inadequate response to antihistamines for the treatment of chronic urticaria. Nevertheless, the findings of this study indicate that a significant proportion of patients who received omalizumab did not require additional treatments, such as antihistamines. Furthermore, among those who required antihistamines, most demonstrated effective symptom control with short-term and low-dose antihistamines. Nevertheless, further research is required to inform the revision of the guidelines.

Ethics

Ethics Committee Approval: This study was approved by Dicle University Non-Interventional Clinical Research Ethics Committee (approval number: 219, date: 17.05.2023).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.İ.G., E.A., Concept: H.İ.G., E.A., Design: H.İ.G., E.A., Data Collection or Processing: H.İ.G., E.A., Analysis or Interpretation: H.İ.G., E.A., Literature Search: H.İ.G., Writing: H.İ.G., E.A.

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