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Omalizumab in Chronic Spontaneous Urticaria: Assessment of Response in Twenty-Five Patients

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ABSTRACT

Background
Omalizumab is a recombinant humanized monoclonal antibody against immunoglobulin E (IgE). It is approved for the treatment of chronic spontaneous urticaria (CSU) in patients ≥12-years of age.

Objective
We carried out a retrospective cross-sectional study in 25 patients with CSU to evaluate the characteristics of response of CSU to omalizumab treatment.

Method
A retrospective cross-sectional study of a convenient sample of all patients diagnosed as CSU who have been using omalizumab treatment during the study period from January 2018 to January 2020 in the Dermatology Department in King Abdulaziz Hospital, Makkah, Saudi Arabia.

Results
A total of 25 patients have participated in this study. The average age of patients was 40-years. Majority of the patients were female (52.0%, n=15). The average duration of illness was 1.32-years. Majority of the patients (72.0%, n=18) received two courses of omalizumab treatment. Minority of patients (28.0%, n=7) received one course of omalizumab treatment which was statistically significant (*p* value<0.01). Number of patients who have been using oral 2nd generation antihistamine during the first course and 2nd course was (72%, n=18 out of 25) and (50%, n=9 out of 18) respectively. Number of flare-ups during 2nd course (1.72 flares up per patient, n=31 flare-ups among 18 patients) was less than the number of flares-up during 1st course (2.96 flares-up per patient, n=74 flare-ups among 25 patients) which was statistically significant (*p* value<0.01). Number of patients who showed no flare-ups during the 1st and 2nd course of omalizumab treatment was (16%, n=4 out of 25 patients) and (27.77%, n=5 out of 18 patients) respectively. The average intensity of flares-up during 2nd course of omalizumab treatment was less than the average intensity of flares-up during first course of omalizumab treatment as the following; during 2nd course (33.33%, n=6 out of 18 patients), (27.77% n=5 out of 18 patients), (11.11%, n=2 out of 18 patients) mild, moderate and severe flares-up respectively and the severity during 1st course was (40.0%, n=10 out of 25 patients), (28.0%, n=7 out of 25 patients), (16.0%, n=4 out of 25 patients) mild, moderate and severe flares-up respectively.

Conclusion
According to expert's guidelines, CSU of ≥3-years would be treated with omalizumab for a minimum of one-year. In our study, in spite of the short duration of CSU (average duration was 1.32-years), the majority of patients (72.0%, n=18) received omalizumab for 1-year (two courses of omalizumab treatment) suggesting that the majority of patients with CSU in general requires omalizumab ≥1-year. Our study also showed 5 patients who were free of any flare-up and they were not using 2nd generation antihistamines suggesting that omalizumab alone as monotherapy can be effective.

Keywords
Omalizumab; Urticaria; RCTs; Chronic spontaneous urticaria (CSU).

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INTRODUCTION

Omalizumab is a recombinant humanized monoclonal antibody against immunoglobulin E (IgE). It is approved for the treatment of chronic spontaneous urticaria (CSU) in patients ≥12-years of age. Mechanism of action of omalizumab is by decreasing serum levels of free IgE and also by down-regulation of the high-affinity IgE receptors on mast cells, basophils, and dendritic cells. The most effective dose of omalizumab is 150-300 mg subcutaneous injection every four weeks.[1,2]

Urticaria is a common inflammatory condition characterized by wheals that last less than 24-hours. When urticaria continues for more than 6-weeks with no apparent cause, it is called CSU. The first line treatment of CSU is 2nd generation anti H1-antihistamine therapy. However, in a significant proportion of patients, symptoms persist despite using the second line treatment (full dose of 2nd generation H1-antihistamines (up to 4 times daily).[2-4] Current global guidelines for the treatment of CSU recommend other add-on therapies as a second or third-line treatment that includes adding omalizumab to the 2nd generation anti H1-antihistamines. After 6-months of omalizumab treatment, omalizumab is usually discontinued. If recurrence occurred, reintroduction of omalizumab treatment is required.[5,6]

We carried out a retrospective cross-sectional study in 25 patients with CSU to evaluate the characteristics of response of CSU to omalizumab treatment. According to expert's guidelines, CSU of ≥3-years would be treated with omalizumab for a minimum of one year. In our study, in spite of the short duration of CSU (average duration was 1.32-years), the majority of patients (72.0%, n=18) received omalizumab for 1-year (two courses of omalizumab treatment) suggesting that the majority of patients in general requires longer treatment period.

METHOD

Study Design and Sample

A retrospective cross-sectional study of a convenient sample of all patients diagnosed with CSU who have been using omalizumab treatment in the study period from January 2018 to January 2020 was conducted in the Dermatology Department at Makkah, Saudi Arabia. The inclusion criteria include patients who have been diagnosed as CSU who are; 1. above 12-years; 2. received omalizumab 300 mg SC injection every month within the study period; 3. should complete the full course (6-months) of omalizumab treatment; 4. Urticaria severity score was recorded in the patient's medical records (Table 1).

Table 1. *Urticaria Severity Score*

Score	Wheal	Pruritus
0	No	No
1	Mild (<20 wheal /24 h)	Present but not troublesome.
2	Moderate (20-50 wheal /24 h)	Troublesome, but not interfere with daily life activity.
3	Intense (>50 wheal/24 h) or large confluent area	Interfere with daily activity

Patients who have incomplete or insufficient clinical data were excluded from the study.

The patient's data were collected from the patient's medical records; age, gender, duration of illness urticaria severity score and use of 2nd generation antihistamines in each patient visit (Table 1).

Statistical Analysis

Data were analyzed using statistical package for the social sciences (SPSS) software, version 22. Descriptive analysis was reported as mean (μ)±SD for normally distributed quantitative variables, and as median (interquartile range) for non-normally distributed quantitative variables. Normality of the data was examined using histogram. Categorical data were reported as frequencies (n) and percentages (%).

RESULTS

Participants' Demographic Characteristics

A total of 25 patients with CSU have participated in this study. The average age of the patients was 40-years (SD=14.26). Majority of the patients were females (43%, n=15). The average of duration of illness was 1.32-years (Table 2).

Effects of the Omalizumab in CSU

Majority of the patients (72.0%, n=18) received two courses of omalizumab treatment. Minority of patients (28.0%, n=7) received one course of omalizumab treatment treatment which was statistically significant (p value<0.01). Number of patients who have been using oral 2nd generation antihistamine during 1st course and 2nd course was (72%, n=18 out of 25) and (50%, n=9 out of 18) respectively.

Number of flare-ups during 2nd course (1.72 flares-up per patient, n=31 flares-up among 18 patients) was less than the number of flares-up during 1st course (2.96 flares-up per patient, n=74 flares-up among 25 patients) which was statistically significant (p value<0.01). Number of patients who showed no flare-ups during the 1st and 2nd course of omalizumab treatment was (16%, n=4 out of 25 patients) and (27.77%, n=5 out of 18 patients) respectively.

The average intensity of flares-up during 2nd course of omalizumab treatment was less than the average intensity of flares-up during 1st course of omalizumab treatment as the following; during 2nd course (33.33%, n=6 out of 18 patients), (27.77%, n=5 out of 18 patients), (11.11%, n=2 out of 18 patients) mild, moderate and severe flares-up respectively and the severity during 1st course was (40.0%, n=10 out of 25 patients), (28.0%, n=7 out of 25 patients), (16.0%, n=4 out of 25 patients) mild, moderate and severe flares-up respectively (Figure 1).

DISCUSSION

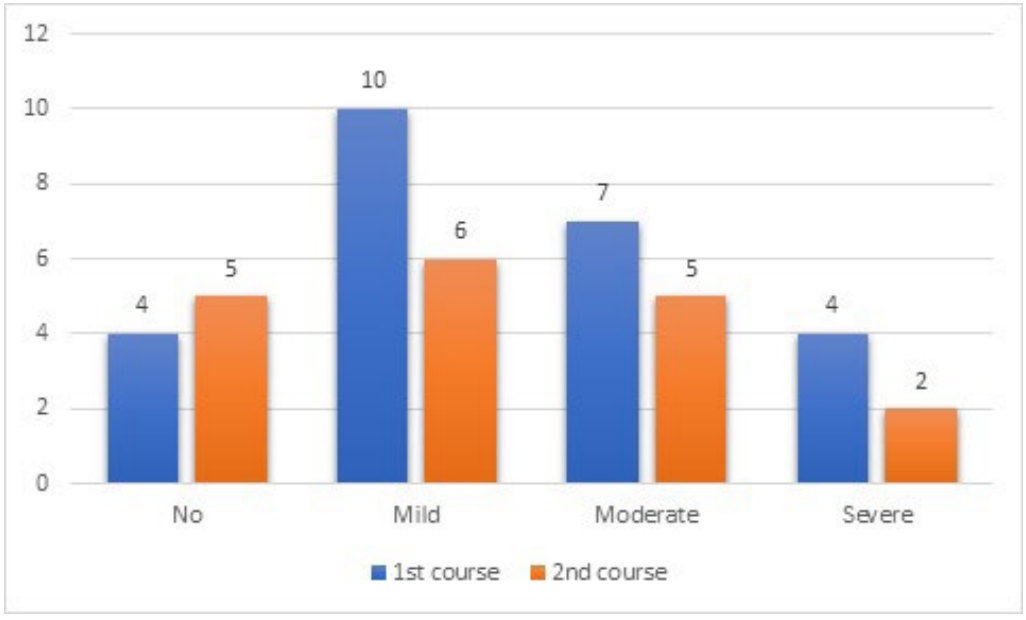
Omalizumab has been shown to be effective in the treatment of

Table 2. *Demographic Data and Characteristics of Response to Omalizumab Treatment in 25 Patients*

Patient Number	Age	Gender	Duration of Illness	Number of Flares up during the 1st Course of Omalizumab	The Average of Urticaria Severity Score during 1st Course of Omalizumab Treatment	2nd Generation Antihistamine Use during 1st Course	Number of Flares up during the 2nd Course of Omalizumab	The Average of Urticaria Severity Score during 2nd Course of Omalizumab Treatment	2nd Generation Antihistamine use during 2nd Course of Omalizumab
1	65	Female	2 Y	6	Severe	Yes	3	Moderate	Yes
2	20	Male	1 Y	4	Moderate	Yes	2	Mild	Yes
3	55	Female	2 Y	0	0	Yes	DR		
4	67	Female	10 M	5	Severe	No	2	Mild	Yes
5	28	Female	5 M	2	Mild	Yes	DR		
6	29	Male	8 M	3	Mild	Yes	0	0	Yes
7	30	Male	2 Y	3	Moderate	Yes	1	Mild	Yes
8	70	Female	2 Y	0	0	Yes	DR	0	
9	45	Female	1 Y	6	Severe	Yes	4	Mild	No
10	22	Male	4 Y	4	Moderate	No	3	Moderate	Yes
11	43	Male	3 M	0	0	Yes	DR		
12	40	Female	2 Y	4	Moderate	Yes	3	Moderate	Yes
13	28	Female	5 M	3	Moderate	No	3	Mild	Yes
14	33	Male	2 Y	1	Mild	Yes	DR		
15	41	Male	5 M	2	Mild	Yes	DR		
16	20	Male	2 Y	3	Moderate	No	0	0	No
17	34	Female	1 Y	3	Moderate	Yes	0	0	No
18	50	Female	4 M	4	Severe	Yes	2	Severe	No
19	55	Male	2 Y	2	Mild	Yes	0	0	No
20	27	Female	1 Y	0	0	No	DR		
21	37	Male	5 M	4	Mild	No	0	0	No
22	39	Female	3 Y	5	Mild	Yes	3	Moderate	No
23	41	Female	5 M	3	Mild	yes	1	Moderate	Yes
24	43	Female	2 Y	2	Mild	No	1	Mild	No
25	52	Female	4 M	5	Mild	yes	3	Severe	No

DR: Did not receive 2ndcourse of omalizumab.Y;Year. M; month

Figure 1. *Severity of Urticaria during Flare-ups Using Severity Score of Urticaria during 1st and 2nd Course of Omalizumab*



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CSU. Our study showed that CSU is common in middle-aged females (like what has been mentioned in the literature. The duration of omalizumab therapy in CSU has not been determined. According to guidelines, CSU of ≥3-years would be treated with omalizumab for a minimum of one year.[5,6]

In our study, in spite of the short duration of CSU (the average duration was 1.32-years), the majority of patients (72.0%, n=18) in our study received omalizumab for 1-year (two courses of omalizumab treatment) suggesting that the majority of patients with CSU in general requires omalizumab ≥1-year.

There are no standard guidelines of omalizumab treatment in CSU. According to some guidelines, omalizumab treatment is used for 6-months, if the patient had complete resolution of symptoms or had very mild symptoms especially at the beginning of the treatment, omalizumab can be discontinued. If recurrence occurred, reintroduction of omalizumab treatment is required.[5,6] In our study, the 7 patients whom did not require a 2nd course of omalizumab treatment were those whom developed mild symptoms only in the first 2-months of omalizumab treatment. Patients whom had moderate-severe flares-up in the last 2-months of the 1st course received the 2nd course immediately without stopping omalizumab. Those whom had mild flares-up in the last 2-months of the 1st course, the omalizumab was stopped and then reintroduced because they got moderate-severe flares-up. This indicates that it is better not to stop omalizumab if the patient has mild flares-up in the last 2-months of omalizumab therapy.

Some experts suggested the following guidelines; If the patient has complete resolution of symptoms for 2-3-months, the dose can be lowered to 150 mg, and the interval between injections can be gradually increased. If a patient has no symptoms for 8-weeks on 150 mg every 8-weeks, omalizumab can be stopped. Other experts maintain a dose of 300 mg monthly, prolong the interval by one week per cycle, and discontinue omalizumab if the patient's disease remains controlled for 8-weeks. For patients with partial responses to omalizumab at 300 mg, there may be further improvement with doses of 450 or 600 mg every month or 150 mg every two-weeks. If the patient has little improvement after 4-months on omalizumab, therapy should be discontinued.[6-9]

Number of flares-up during 2nd course (1.72 flares-up per patient, n=31 flares-up among 18 patients) was less than the number of flares-up during 1st course (2.96 flares-up per patient, n=74 flares-up among 25 patients) which was statistically significant (p value<0.01). These findings are similar to RCT results in the literatures.[6-8]

We have noted that patients who were receiving oral 2nd generation anti-histamines plus omalizumab treatment (during both 1st and 2nd courses of omalizumab treatment) were having less flare-ups which are similar to RCT results mentioned in the literatures.[6-8]

Our study also showed that omalizumab alone as monotherapy without adding 2nd generation antihistamines can be effective as there was one patient (patient # 20) during 1st course and 4 patients during the 2nd course (patients # 16,17,19 and 22) who did not get any flare-up and they were not using 2nd generation antihistamines.

Among patients who developed flare-ups during 1st course, the majority of them were mild (40.0%, n=10 out of 25 patients) or moderate (28.0%, n=7 out of 25 patients) and also majority of patients during the 2nd course were mild (33.33%, n=6 out of 18 patients) or moderate (27.77%, n=5 out of 18 patients) which are similar to RCT results in the literatures.[6-8]

Our study showed that numbers of flares-up during omalizumab treatment is proportional to the need for 2nd course of omalizumab. Patients who did not require a 2nd course of omalizumab treatment were those who were having less than 2 flare-ups.

CONCLUSION

According to expert's guidelines, CSU of ≥3-years would be treated with omalizumab for a minimum of one-year. In our study, in spite of the short duration of CSU (average duration was 1.32-years), the majority of patients (72.0%, n=18) received omalizumab for 1-year (two courses of omalizumab treatment) suggesting that the majority of patients in general requires longer treatment period. Our study also showed 5 patients who were free of any flare-up by using omalizumab alone without using 2nd generation antihistamines suggesting that omalizumab alone as monotherapy can be effective.

ETHICAL CONSIDERATION

The approval was obtained from Institutional Review Board (IRB), King Abdul Aziz Hospital, Makkah, Saudi Arabia. All the collected data kept confidential.

CONSENT

An informed consent was obtained from all the participants.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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