

Original Research Article

Evaluation of omalizumab at certain time intervals in patients with chronic spontaneous idiopathic urticaria

Ömer Kutlu^{1*}, Engin Karaarslan², Nermin Karaosmanoğlu³, Hatice Meral Ekşiöğlü³

Department of Dermatology and Venereology, ¹Kayseri Develi State Hospital, Kayseri, ²Mardin Nusaybin State Hospital, Mardin, ³Ankara Training and Research Hospital, Ankara, Turkey

Received: 23 September 2019

Revised: 11 November 2019

Accepted: 13 November 2019

***Correspondence:**

Dr. Ömer Kutlu,

E-mail: omerkutlu22@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: In this study, we aimed to evaluate the response of patient treated with omalizumab at certain time intervals through 6 months with pruritus visual analog scale, urticaria activity score and quality of life indexes.

Methods: The study was performed on ten patients diagnosed with chronic idiopathic spontaneous urticaria. The disease was assessed by the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) and Dermatology Life Quality Index (DLQI) for every 2 weeks while was assessed by Urticaria Activity Score (UAS-7) and Pruritus Visual Analog Scale (PVAS) for once a week during the 6-month treatment period. Statistical significance was evaluated using the Mann-Whitney *U* test in SPSS 20.

Results: Pre-treatment values of the DLQI, CU-Q2oL, UAS-7, and PVAS was statistically higher than post-treatment values of these indexes ($p < 0.05$). The mean DLQI/ CU-Q2oL value of the patients before treatment was $17 \pm 6.09 / 52.87 \pm 22.07$ while it was 19.4 ± 16.36 at the end of 2nd-week post-injection per month, and was 21.85 ± 16.56 at the end of 4nd-week post-injection per month during 6-months following. Statistically, PVAS score at the 4th week was higher than 2nd and 3rd weeks ($p < 0.042$, $p < 0.007$).

Conclusions: In this study, it was detected that omalizumab had a significant effect on DLQI, CU-Q2oL, UAS-7, PVAS scores in CISU. It can be concluded that significant increase of PVAS score at 4th week compared to scores at 2nd and 3rd week may necessitate the use of omalizumab combined with antihistamines at 4th week of the treatment.

Keywords: Life quality, Omalizumab, Pruritus visual analog scale, Urticaria

INTRODUCTION

Urticaria is a mast-cell related skin disease. It is defined as recurrence of hives, angioedema, or both that impairs quality of life.¹ Urticaria lasting for more than 6 weeks is termed chronic urticaria. Chronic urticaria is divided into two groups that consist of spontaneous or inducible.² Most patients with chronic urticaria are diagnosed without identifiable cause known as chronic idiopathic spontaneous urticaria (CISU).³ It is known that in 30-50% of the patients with chronic urticaria including functional

autoantibodies against IgE or the alpha subunit of the high-affinity immunoglobulin E (IgE) receptor.⁴

Treatment of the urticaria including first- and second-generation H1-antihistamines, cyclosporine, montelukast, corticosteroids, and omalizumab.⁵ Omalizumab is a widely used agent in the treatment of CISU. It is a recombinant DNA-derived humanized monoclonal IgE specific, IgG1 J antibody that targets circulating free IgEs.⁶ The EAACI / GALEN / EDF / WAO guideline now introduces omalizumab as the second step in the treatment of H1-antihistamines-resistant CISU.⁷

In this study, we aimed to evaluate the effect of omalizumab at certain time intervals with pruritus visual analog scale (PVAS), urticaria activity score (UAS-7) and quality of life indexes.

METHODS

The study was performed on patients diagnosed with CISU older than 12 years who had failed to treatment four times a day second-generation non-sedating H1 antihistamines in Ankara Training and Research Hospital during January 2015-January 2018. All patients received omalizumab subcutaneously every 4 weeks for 24 weeks. The responses to omalizumab were described as a condition with no symptoms and no necessity for any treatments at least 4 weeks. After 24 weeks treatment of all patients were switched to antihistamines once daily due to the insurance policy. Patients under 12 years of age, mental retardation and receiving any other treatment due to CISU were excluded from this study.

The disease was assessed by the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) and the Dermatology Life Quality Index (DLQI) for every 2 weeks while was assessed by Urticaria Activity Score (UAS)-7 and Pruritus Visual Analog Scale (PVAS) for once a week during the 6-month treatment period. Urticaria Activity Score -7 is the sum of the scores of daily urticaria activity in the last 7 days, it is range from 0–42 points per week; DLQI which is a life quality scale that includes 10 items. A total score of DLQI ranges from 0–30. A high score shows a disrupt in a life quality; CU-Q2oL consist of physical, emotional, social and practical fields that characterize urticaria; PVAS is a common method for pruritus severity evaluation, as it provides an easy and quick prediction of itch. It is ranged from 0-10.^{8,9}

The 6-month following data of the patients were analyzed with SPSS 20. The means±standard deviation (SD) was used for descriptive statistics. Statistical significance was

evaluated using the Mann-Whitney *U* test. *p* values <0.05 were considered to describe statistical significance.

RESULTS

Nine of the patients were female and one of the patients was a male with a mean age of 40.6 (minimum 20, maximum 50). The mean value of disease duration was 31.79±3.70 (minimum 2, maximum 13) years. Pre-treatment scores of the DLQI, CU-Q2oL, UAS-7, and PVAS was statistically higher than post-treatment scores of these indexes (*p*<0.05) (Table 1).

The mean DLQI score of the patients before treatment was 17±6.09 (minimum 6, maximum23). After initiation of omalizumab, the mean DLQI score at the 2nd-weeks post-injection was 4.29±5.1 (minimum 0, maximum 13) while at the 4th-weeks post-injection was 5.09±3.9 (minimum 0 to maximum 12). In addition, the mean CU-Q2oL score of the patients before treatment was 52.87±22.07 (minimum 27.7, maximum 81.5). On the other hand, it was 19.4±16.36 (minimum 0, maximum 45.1) and was 21.85±16.56 (minimum 27.7, maximum 81.5) after 2nd-weeks and 4th-weeks post-injection of omalizumab, respectively.

Table 1: Demographic and clinical characteristics of patients receiving omalizumab.

Female, N (%)	9 (90)
Mean age (min, max) (years)	40.6±9.78 (20, 56)
Mean body mass index value (min, max) kg/m²	31.79±7.21 (23.63, 44.79)
Mean duration of disease (years)	31.79±3.70 (2, 13)
Pre-treatment DLQI score (min, max)	17±6.09 (6, 23)
Pre-treatment CU-Q2oL (min, max)	52.87±22.07 (27.7, 81.5)
Pre-treatment PVAS (min, max)	8.67±1.2 (7, 10)

min: minimum max: maximum.

Table 2: Changes in PVAS score during omalizumab treatment.

	Post-treatment-PVAS		
	Minimum	Maximum	Mean±SD
1st week	0	7.80	2.66±2.68
2nd week	0	4.75	2.14±1.99
3rd week	0	5.00	2.36±2.13
4th week	0	7.00	3.46±2.38

Std.: standard deviation; PVAS: Pruritus Visuale Analog Scale.

Table 3: Changes in UAS during omalizumab treatment.

	Post-treatment-UAS7		
	Minimum	Maximum	Mean±SD
1st week	0	36.25	11.32±12.66
2nd week	0	20.75	7.83±7.64
3rd week	0	21.00	9.40±9.21
4th week	0	23.25	10.14±9.12

Std.: standart deviation; UAS7: Urticaria Activity Score.

There was no statistically significant difference between the mean DLQI scores of the 2nd week and 4th week after injection for 6 months. Similarly, there was no statistically significant difference between the mean CU-Q2oL score of the 2nd week and the mean CU-Q2oL score of the 4th week after omalizumab injection for 6-month follow-up period.

Pre-treatment PVAS score was 8.66 ± 1.21 (minimum 7, maximum 10) and was statistically higher than post-treatment 6-months mean PVAS score. Furthermore, there was a significant difference between 2nd and 4th week and also between 3rd and 4th week according to the PVAS score that evaluated every week ($p < 0.042$, $p < 0.007$). Statistically, PVAS score at the 4th week was higher than in other weeks (Table 2). Pre-treatment UAS-7 score was 37.33 ± 6.02 (minimum 28, maximum 42). It was statistically higher than post-treatment 6-months mean UAS-7 score (Table 3).

DISCUSSION

Omalizumab is a biological agent that provides improvement in disease activity and patient quality of life in the treatment of CISU.¹⁰ All patients in this study were resistant to antihistamine treatment with dosages up to fourfold and all were treated with omalizumab. DLQI, CU-Q2oL, UAS-7, and PVAS scores of all patients who received 300 mg subcutaneously omalizumab per month improved significantly. Although previous studies have shown the effect of omalizumab on quality of life in the last month of treatment, no studies have been conducted on the evaluation of the quality of life regularly in the treatment process.¹¹⁻¹³ In this study, mean scores of DLQI and CU-Q2oL of the patients were evaluated in every session of 2nd week and 4th week after omalizumab injection for 6 months. The mean DLQI score of the patients was 17 before the treatment. On the other hand, it was 4.29 and 5.09 at the end of 2nd and 4th-week post-injection of omalizumab for 6 months, respectively, that was consistent with data reported in the literature.¹⁴ When the DLQI score was examined, it was found that the quality of life on the 2nd week was higher than the fourth week but it was not statistically significant. Similarly, after follow-up 6 months the mean CU-Q2oL score which was 52.87 before the treatment decrease to 21.85 at the end of 2 weeks after omalizumab injection and 19.14 at the end of 4 weeks after omalizumab injection. In this regard it can be concluded that 1-month treatment interval with omalizumab is enough in terms of quality of life index.

In previous studies, the relationship between omalizumab and itching was mostly performed with Itch Severity Score (ISS). The weekly ISS including the average daily sum of pruritus scores in the last 7 days with a range from 0 to 21.¹⁵ Of these studies, Saini et al. reported that the mean change in ISS was -9.2 ± 5.98 with 300 mg omalizumab treatment. In other two studies, it was reported that change in ISS was -9.8 ± 6.0 and -9.4 ± 5.73 in

patients receiving 300 mg omalizumab while it was -8.1 ± 6.4 and -6.66 ± 6.28 , respectively, in patients receiving 150 mg omalizumab.¹⁶⁻¹⁸ These results can indicate that the dose-dependent itching score decreases with omalizumab treatment. In our study, patients were evaluated for weekly PVAS score for 6 months. The mean PVAS score at 4 weeks after omalizumab injection was higher than the first 3 weeks for 6 months. Furthermore, the PVAS score of the 4th week was significantly higher than the PVAS score of 2nd and 3rd week. The UAS7 score had the highest value at 1st and 4th week, although there was no significant difference compared to other two weeks. In this regard, it can be speculated that decreasing treatment interval of omalizumab could decrease more pruritus and UAS-7. This result may provide a different approach to the treatment of omalizumab compared with previous dose-dependent studies in term of itching score.

In addition, it could be concluded that antihistamines can be added to the current treatment in patients with high 4th-week pruritus and UAS-7 score. This parameter can be used in addition to present algorithms in the individual approach in the treatment of Omalizumab.¹⁹ The topic should be elucidated by further studies that including a large sample size.

CONCLUSION

In this study, it was detected that omalizumab had a significant effect on DLQI, CU-Q2oL, UAS-7, PVAS scores in CISU. It can be concluded that significant increase of PVAS score at 4th week compared to scores at 2nd and 3rd week may necessitate the use of omalizumab combined with antihistamines at 4th week of the treatment.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Kolkhir P, Church MK, Weller K, Metz M, Schmetzer O, Maurer M. Autoimmune chronic spontaneous urticaria: what we know and what we do not know. *J Allergy Clin Immunol.* 2017;139(6):1772-81.
2. Kaplan AP. Chronic spontaneous urticaria: pathogenesis and treatment considerations. *Allergy Asthma Immunol Res.* 2017;9(6):477-82.
3. Kavati A, Zhdanova M, Ortiz B, LeCocq J, Schiffman B, Pilon D, et al. Long-term omalizumab outcomes in chronic idiopathic urticaria: a real-world study. *Allerg Asthma Proc.* 2019;40(5):321-8.
4. Sheikh J. Autoantibodies to the high-affinity IgE receptor in chronic urticaria: how important are they? *Curr Opin Allergy Cl, 2005;5(5):403-7.*

5. Maurer M, Metz M, Brehler R, Hillen U, Jakob T, Mahler V, et al. Omalizumab treatment in patients with chronic inducible urticaria: a systematic review of published evidence. *J Allergy Clin Immunol.* 2018;141(2):638-49.
6. Vichyanond P. Omalizumab in allergic diseases, a recent review. *Asian Pac J Allergy Immunol.* 2011;29:209.
7. Zuberbier T, Aberer W, Asero R, Abdul Latiff AH, Baker D, Ballmer-Weber B, et al. The EAACI/GA²LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. *Allergy.* 2018;73(7):1393-414.
8. Langner M, Maibach H. Pruritus measurement and treatment. *Clin Experiment Dermatol.* 2009;34(3):285-8.
9. Kocatürk E, Weller K, Martus P, Aktas S, Kavala M, Sarigul S, et al. Turkish version of the chronic urticaria quality of life questionnaire: cultural adaptation, assessment of reliability and validity. *Acta Derm Venereol.* 2012;92(4):419-25.
10. Ertaş R, Ozyurt K, Atasoy, Hawro T, Maurer M. The clinical response to omalizumab in chronic spontaneous urticaria patients is linked to and predicted by IgE levels and their change. *Allergy.* 2018;73(3):705-12.
11. Büyükoztürk S, Gelincik A, Demirtürk M, Kocaturk E, Colakoğlu B, Dal M. Omalizumab markedly improves urticaria activity scores and quality of life scores in chronic spontaneous urticaria patients: a real life survey. *J Dermatol.* 2012;39(5):439-42.
12. Janssens N, Maurer M, Khalil S, Balp MM, Rosen K. Omalizumab Improves Quality of Life (QoL) in Patients with Chronic Spontaneous/Idiopathic Urticaria (CSU/CIU) As Assessed By the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL): A Post-Hoc Analysis of Percent Change from Baseline to Week 12. *J Allergy Clin Immunol.* 2015;135(2):AB132.
13. Staubach P, Metz M, Chapman-Rothe N, Sieder C, Brautigam M, Maurer M, et al. Omalizumab rapidly improves angioedema-related quality of life in adult patients with chronic spontaneous urticaria: X-ACT study data. *Allergy.* 2018;73(3):576-84.
14. Bulur I, Bulbul Baskan E, Ozdemir M, Balevi A, Kocatürk E, Altunay I, et al. The efficacy and safety of omalizumab in refractory chronic spontaneous urticaria: real-life experience in Turkey. *Acta Dermatovenerol Alp Pannonica Adriat.* 2018;27(3):121-6.
15. Carrillo DC, Borges MS, Garcia E, Egae E, Serrano CD. Omalizumab vs. placebo in the management of chronic idiopathic urticaria: a systematic review. *World Allergy Organ J.* 2014;7(1):72.
16. Saini S, Rosen KE, Hsieh HJ, Wong DA, Conner E, Kaplan A, et al. A randomized, placebo-controlled, dose-ranging study of single-dose omalizumab in patients with H1-antihistamine-refractory chronic idiopathic urticaria. *J Allergy Clin Immunol.* 2011;128(3):567-73.
17. Maurer M, Rosén K, Hsieh HJ, Saini S, Grattan C, Gimenez-Arnau A, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. *New Engl J Med.* 2013;368(10):924-35.
18. Saini SS, Bindslev-Jensen C, Maurer M, Grob J, Bülbül Başkan E, Bradley MS, et al. Efficacy and safety of omalizumab in patients with chronic idiopathic/spontaneous urticaria who remain symptomatic on H1 antihistamines: a randomized, placebo-controlled study. *J Invest Dermatol.* 2015;135(1):67-75.
19. Uysal P, Eller E, Mortz CG, Bindsley-Jensen C. An algorithm for treating chronic urticaria with omalizumab: dose interval should be individualized. *J Allergy and Clin Immunol.* 2011;133(3):914-15.

Cite this article as: Kutlu Ö, Karaarslan E, Karaosmanoğlu N, Ekşioğlu HM. Evaluation of omalizumab at certain time intervals in patients with chronic spontaneous idiopathic urticaria. *Int J Sci Rep* 2019;5(12):351-4.