NEÜ PRESS

MEVLANA TIP BİLİMLERİ
MEVLANA MEDICAL SCIENCES
eISSN:2757-976X

ARAŞTIRMA MAKALESİ/RESEARCH ARTICLE

Mev Med Sci, 2021; 1(2): 37-41

# Effects of Omalizumab Treatment on Hematological Parameters and Total IgE Levels in Patients with Chronic Idiopathic Urticaria

## Kronik İdiyopatik Ürtikerli Hastalarda Kullanılan Omalizumab Tedavisinin Hematolojik Parametreler ve Toplam IgE Düzeylerine Etkileri

İlkay Özer[1]

[1]Necmettin Erbakan University, Meram Faculty of Medicine, Department of Dermatology and Venerology, Konya, Turkey

**Makale Tarihleri/Article Dates:**
**Geliş Tarihi/Recived:** 22 Nisan 2021
**Kabul Tarihi/Accepted:** 24 Haziran 2021
**Yayın Tarihi/Published Online:** 4 Ağustos 2021

**Sorumlu Yazar/Corresponding Author:**
İlkay Özer,
Necmettin Erbakan University, Meram Faculty of Medicine, Department of Dermatology and Venerology, Konya, Turkey
**e mail:** ilkay_8@yahoo.com

**Açıklama/Disclosure:** None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this article. The research was not sponsored by an outside organization. All authors have agreed to allow full access to the primary data and to allow the journal to review the data if requested.

**ÖZET**

**Amaç:** Omalizumab, IgE reseptörüne bağlanan insanlaştırılmış bir antikordur ve kronik ürtikerin tedavisinde etkili olmasına rağmen etki mekanizması hala tam olarak anlaşılamamıştır. Bu çalışmada amacımız, kronik ürtikerli hastalara uygulanan omalizumab tedavisinin, hematolojik parametrelere ve IgE değerleri üzerindeki etkilerini araştırmaktır.

**Gereçler ve Yöntem:** Çalışmamızda kronik ürtiker nedeniyle 3 kür omalizumab tedavisi alan 36 hastanın hematolojik parametreleri ve IgE değerleri tedavi öncesi ve sonrası kaydedildi.

**Bulgular:** Omalizumab tedavisi öncesinde kontrol grubuna göre kronik ürtikerli hastalarda nötrofil-lenfosit oranı daha yüksek (p: 0,038) ve ortalama trombosit hacmi daha düşük (p: 0,01) bulundu. Tedavi sonrası 12 hafta omalizumab tedavisi alan kronik ürtikerli hastaların nötrofil-lenfosit oranı değerlerinin düştüğü (p: 0.05), trombosit dağılım genişliği değerlerinin yükseldiği (p: 0.002) gözlendi. ortalama Orombosit hacmi açısından kronik ürtikerli hastalar ile kontrol grubu arasında anlamlı bir fark gözlenmedi ve tedavi sonunda önemli bir değişiklik olmadı. Hasta grubunda omalizumab tedavisi öncesi IgE değerleri 12. haftadaki IgE değerlerinden yüksekti (p: 0.001).

**Sonuç:** Veriler ışığında, bulgularımız nötrofil-lenfosit oranı, trombosit dağılım genişliği ve toplam IgE değerlerinin kronik ürtikerli hastalarda remisyonun değerlendirilmesi ve takibinde yararlı hematolojik parametreler olabileceğini düşündürmektedir

**Anahtar Kelimeler:** Ig E, Omalizumab, Ürtiker

**ABSTRACT**

**Aim:** Omalizumab is a humanized antibody that binds to the IgE receptor and its mechanism of action is still not fully understood although it is effective in the treatment of chronic urticaria. In this study, our aim is to investigate the effects of omalizumab treatment applied to patients with chronic urticaria on the hematological parameter and on IgE values.

**Materials and Methods:** In our study, the hematological parameter and IgE values of 36 patients, who received three cycles of omalizumab treatment due to chronic urticaria, were recorded before and after the treatment.

**Results:** Before the omalizumab treatment, neutrophil-lymphocyte ratio was found to be higher (p: 0.038), and platelet distribution width was found to be lower (p: 0.01) in patients with chronic urticaria than in the control group. After the treatment, neutrophil-lymphocyte ratio values of the patients with chronic urticaria, who received omalizumab treatment for 12 weeks, were observed to decrease (p: 0.05), and platelet distribution width values were observed to increase (p: 0.002). No significant difference was observed between the patients with chronic urticaria and the control group regarding mean platelet volume, and there was no significant change at the end of the treatment. In the patient group, the IgE values before omalizumab treatment were higher than the IgE values at the 12th week (p: 0.001).

**Conclusion:** In light of data, our findings suggest that neutrophil-lymphocyte ratio, platelet distribution width and IgE values may be useful hematologic parameters for the evaluation and follow-up of remission in patients with chronic urticaria.

**Key words:** Ig E, Omalizumab, Urticaria

**Atıf yapmak için/ Cite this article as:** Özer İ. Effects of Omalizumab Treatment on Hematological Parameters and Total IgE Levels in Patients with Chronic Idiopathic Urticaria. Mev Med Sci. 2021;1(2): 37-41

## INTRODUCTION

Chronic spontaneous urticaria (CSU), which manifests as itchy, raised, and red bumps, is a disease with recurrent episodes occurring at least twice a week for more than 6 weeks (1). Although the primary reason for the release of histamine from mast cells is believed to be due to the proinflammatory, autoimmune, and coagulation pathways involved in the mechanism of the disease, the etiology of CSU is still unclear (2, 3).

Several studies have shown that the levels of inflammatory markers are increased in patients with chronic spontaneous urticaria (4-7). It is known that platelets are involved not only in hemostasis and thrombosis but also in inflammation and immunity (8-10). Platelets have been shown to release histamine (11-12) and to express both high-affinity and low-affinity IgE receptors at different levels (13). Omalizumab, which is used in the treatment of CSU and some studies have reported that omalizumab reduces the level of hemostatic parameters, such as D-dimer, and regresses inflammatory parameters in the treatment of CSU (14,15).

The neutrophil:lymphocyte ratio (NLR) is a hemogram test that is calculated by dividing the total number of neutrophils by the total number of lymphocytes, and it is an easy test to demonstrate systemic inflammation (16).

Mean platelet volume (MPV) is a common measure of platelet size, and platelet distribution width (PDW) is the platelet size heterogeneity index. These parameters have been found to be directly related to the metabolic activities of the platelets (17). It has also been reported that PDW could be used as a marker in the inflammatory response as a negative acute-phase reactant (18,19).

In this study, we investigated the effect of omalizumab used in the treatment of chronic urticaria on NLR, MPV, PDW and total IgE levels.

## MATERIALS AND METHODS

After receiving approval from the local ethics committee, 32 patients with CSU who received three courses of omalizumab treatment and 36 patients controls over were recruited from patients who had been referred for minor dermatological problems, such as tinea pedis and nevus. In our study who has diabetes mellitus, familial hypercholesterolemia, neoplastic diseases, obesity, liver and kidney diseases and recent major surgical procedures were excluded.

Assessment of disease activity in spontaneous urticaria was done using urticaria activity score (UAS). The UAS consists of a total score calculated during the last 7 days, in which the patient provides 0–3 points indicating two major urticaria symptoms, pruritus, and wheals, for each day.

NRL, MPV, PDW, and total IgE (using nephalometrically method) values before omalizumab treatment and at the 12th week of treatment, which were obtained from the medical files of the 32 patients who had received omalizumab treatment, were retrospectively recorded.

The NRL, MPV, and PDW values of age- and gender-matched 36 individuals who applied to the dermatology clinic as a control group were retrospectively analyzed.

Statistical analysis was performed using SPSS version 20.0 software (IBM Corporation, Armonk, NY, USA). The compatibility of the variables to the normal distribution was tested using a one-sample Kolmogorov–Smirnov test. The variables with normal distribution were expressed by mean and standard error (mean ± SE). Chi-square test and Student's independent t-test were used for statistical analysis. A p value of $<0.05$ was considered as statistically significant.

## RESULTS

Among the 32 patients including in this study, 27 (84.4%) patients were females and 5 (15.6%) were males. The mean age of the patients was 47.64 ± 13.08 (range, 26-70)years. In the gender- and age-matched control group consisting of 36 patients, there were 31 (86.1%) females and 5 (13.8%) males, and their mean age was 46.86 ± 12.54 (range, 26-69) years, with no difference in age and gender distribution between the groups. The mean duration of disease in patients with CSU was 53 ± 40 months (range: 7–136 months), and the mean UAS values were 31.8 ± 3.47 (range: 26–40) before omalizumab treatment and 1.88 ± 2.53 (range: 0–8) after omalizumab treatment. Comparison of NRL, MPV, and PDW values between the control group and the CSU group before omalizumab treatment showed that NRL values were significantly higher in the CSU group than those in the control group ($P = 0.043$). There was no significant difference between the patients with CSU and the control group ($P = 0.098$) regarding MPV, whereas the PDW value was found to be lower in patients with CSU ($P = 0.016$) (Table 1). The NRL values of patients with CSU who received omalizumab treatment were significantly lower at the end of the treatment ($P = 0.034$), whereas the PDW values were found to be increased ($P = 0.018$), and no significant difference was observed between the groups in terms of NLR, MPV, and PDW values after the treatment (Table 2). A significant increase in IgE levels was observed in patients with CSU through the 12-week omalizumab treatment period ($P < 0.001$) (Table 2).

## DISCUSSION

CSU, whose etiopathogenesis has not yet been completely understood, is an inflammatory disease characterized by an acute-phase response, and the increase in the levels of inflammatory parameters has been found to be associated with the severity of the disease (5-7, 20,21). Inflammatory markers were observed to be regressed through omalizumab

**Table 1.** NRL, MPV, and PDW values of the control group and the patient group before omalizumab treatment

| | Patient group | Control group | P |
|---|---|---|---|
| NLR | 2.33 ± 1.55 | 1.77 ± 0.5 | 0.043 |
| PDW/ 10(GSD) | 13.5 ± 3.07 | 16.79 ± 7.24 | 0.016 |
| MPV/ fL | 9.93 ± 1.37 | 9.29 ± 1.70 | 0.098 |

treatment that are used in the treatment of CSU (15). NLR is an easy test that can be calculated by dividing the number of neutrophils by the number of lymphocytes, and it is a more significant inflammatory marker than individual measurements of neutrophil and lymphocyte counts. NLR has also been reported to increase in several diseases such as malignant diseases, diabetes mellitus (22-24). NLR has also been reported to increase in dermatological diseases such as psoriasis, atopic dermatitis, bullous pemphigoid, Behcet's disease, and cutaneous vasculitis (25-28). In our study, NLR was significantly higher in the patient group before the treatment than that in the control group. In our study, NLR was observed to be significantly decreased during the 12-week omalizumab treatment period, and the values were found to decrease to the values of the control group. This result may support that omalizumab has an anti-inflammatory effect and that NLR can be used as a marker in CSU treatment follow-up.

The literature reports that coagulation pathway activation has a role in the pathogenesis of chronic urticaria (29-31). The importance of platelets in CSU, which are involved not only in hemostasis but also in vessel repair, tumor growth, inflammation, and immunity, has been increasingly clarified in several studies (29,32,33). It has been reported that MPV and PDW values could be used as an easy marker of platelet activation (17). MPV, which is a marker of platelet size and activation, was observed to increase in inflammatory diseases such as psoriasis, Pemphigus Vulgaris, rheumatoid arthritis, and malignancies and has been reported to be a marker associated with disease activation (34-38). Data regarding MPV values in chronic urticaria are contradictory. Some studies have reported that MPV values were lower than those in the control group in chronic spontaneous urticaria (33,39), whereas other studies have reported an increase or not different (40-42). In our study, no difference was observed in the patient group with chronic urticaria compared to that in the control group in terms of MPV. Studies carried out on patients with rheumatoid arthritis and fibromyalgia have suggested PDW as an inflammatory marker and that it can be used as a negative acute-phase reactant (18,19). There are also contradictions in studies investigating PDW values. In a study by Chandrashekar et al. (41), the PDW values of 45 patients with CSU were found to be higher than those in the control group. However, Isıksacan et al. (33) reported no significant difference in PDW values in 34 patients with CSU, and similarly, Kasperska-Zajac et al. (40) also reported no difference in 66 patients. In our study, PDW was found to be lower in the control group compared to the control group and it was observed that after the treatment with omalizumab, the control group had increased to similar values. This condition may suggest that PDW is a negative acute-phase reactant as in previous study. This may be due to the anti-inflammatory effect of omalizumab in the remission of CSU, which is responsible for the inflammation in its etiology.

**Table 2.** Post-treatment NRL, MPV, PDW, and total IgE values of the patients who received omalizumab treatment (NLR: neutrophil: lymphocyte ratio, PDW: platelet distribution width, MPV: mean platelet volume)

| | Before Omalizumab Treatment | After Omalizumab Treatment | P |
|---|---|---|---|
| NLR | 2.33 ± 1.55 | 1.92 ± 1.10 | 0.034 |
| PDW/ 10(GSD) | 13.5 ± 3.07 | 14.68 ± 2.79 | 0,018 |
| MPV/fL | 9.93 ± 1.37 | 9.77 ± 1.74 | 0,484 |
| Total IgE/IU/mL | 110.12 ± 90,01 (min:17 max:1110) | 340.40±257.05 (min:18.5 max:3180) | <0,001 |

The effects of omalizumab treatment on total IgE levels in patients with chronic urticaria show conflicting results. One study reported that the total IgE levels decreased after omalizumab treatment (43). In a double-blind, randomized trial conducted by Metz et al. (44) in which 30 patients with CSU who received 12-week omalizumab treatment were examined, the total IgE level was reported to increase until the 12th week of the treatment, whereas free IgE levels were reported to decrease significantly with the first dose and then plateau (44). In another study by Ertaş et al. (45) involving patients with CSU, in which the relationship between response to omalizumab treatment and IgE levels was investigated, a significant increase in total IgE levels was observed in patients who responded to the treatment (45). In our study, the total IgE levels were observed to be increased in patients with partial or complete remission with omalizumab treatment.

In conclusion, Decreases in NLR and increases in PDW due to omalizumab treatment support the anti-inflammatory effect of omalizumab in the treatment of CSU. We believe that NLR, PDW, and total IgE levels may be used as objective markers for the follow-up of remission during omalizumab treatment of CSU.

***Conflict of interest:*** Authors declare that there is no conflict of interest between the authors of the article.

***Financial conflict of interest:*** Authors declare that they did not receive any financial support in this study.

***Corresponding Author:*** *İlkay Özer, Necmettin Erbakan University, Meram Faculty of Medicine, Department of Dermatology and Venerology, Konya, Turkey*
***Telefon:*** *+90505 2584264*
***e-mail:*** *ilkay_8@yahoo.com*

**REFERENCES**

1. Kulthanan K, Tuchinda P, Chularojanamontri L, et al. Clinical practice guideline for diagnosis and management of urticaria. Asian Pacific journal of allergy and immunology 2016;34:190-200.
2. Asero R, Tedeschi A, Marzano AV, et al. Chronic urticaria: A focus on pathogenesis. F1000Research 2017; 6:1095.
3. Asero R, Tedeschi A, Coppola R, et al. Activation of the tissue factor pathway of blood coagulation in patients with chronic urticaria. The Journal of allergy and clinical immunology 2007; 119:705-10.
4. Kolkhir P, Andre F, Church MK, et al. Potential blood biomarkers in chronic spontaneous urticaria. Clinical and experimental allergy: Journal of the British Society for Allergy and Clinical Immunology 2017;47:19-36.
5. Kasperska-Zajac A, Grzanka A, Machura E, et al. Increased serum complement C3 and C4 concentrations and their relation to severity of chronic spontaneous urticaria and CRP concentration. Journal of inflammation 2013;10:22.
6. Kasperska-Zajac A, Grzanka A, Machura E, et al. Analysis of procalcitonin and CRP concentrations in serum of patients with chronic spontaneous urticaria. Inflammation research : Official journal of the European Histamine Research Society [et al] 2013;62:309-12.
7. Ucmak D, Akkurt M, Toprak G, et al. Determination of dermatology life quality index, and serum C-reactive protein and plasma interleukin-6 levels in patients with chronic urticaria. Postepy dermatologii i alergologii 2013;30:146-51.
8. Kapur R, Zufferey A, Boilard E, et al. Nouvelle cuisine: Platelets served with inflammation. Journal of immunology 2015;194:5579-87.
9. Jenne CN, Kubes P. Platelets in inflammation and infection. Platelets 2015; 26:286-92.
10. Habets KL, Huizinga TW, Toes RE. Platelets and autoimmunity. European journal of clinical investigation 2013;43:746-57.
11. Jancinova V, Nosal R. Increased histamine content in Ca2+-ionophore A23187-activated human blood platelets. Platelets 1998;9:203-6.
12. Masini E, Di Bello MG, Raspanti S, et al. The role of histamine in platelet aggregation by physiological and immunological stimuli. Inflammation research: Official journal of the European Histamine Research Society [et al] 1998;47:211-20.
13. Joseph M, Gounni AS, Kusnierz JP, et al. Expression and functions of the high-affinity IgE receptor on human platelets and megakaryocyte precursors. European journal of immunology 1997;27:2212-8.
14. Asero R, Marzano AV, Ferrucci S, et al. D-Dimer plasma levels parallel the clinical response to omalizumab in patients with severe chronic spontaneous urticaria. Int Arch Allergy Immunol 2017; 172: 40-44.
15. Altrichter S, Hawro T, Hanel K, et al. Successful omalizumab treatment in chronic spontaneous urticaria is associated with lowering of serum IL-31 levels. Journal of the European Academy of Dermatology and Venereology: JEADV 2016;30:454-5.
16. Chandrashekara S, Mukhtar Ahmad M, Renuka P, et al. Characterization of neutrophil-to-lymphocyte ratio as a measure of inflammation in rheumatoid arthritis. International journal of rheumatic diseases 2017;20:1457-67.
17. Vagdatli E, Gounari E, Lazaridou E, et al. Platelet distribution width: A simple, practical and specific marker of activation of coagulation. Hippokratia 2010;14:28-32.
18. Akturk S, Buyukavci R. Evaluation of blood neutrophil-lymphocyte ratio and platelet distribution width as inflammatory markers in patients with fibromyalgia. Clinical rheumatology 2017; 36:1885-9.
19. Isik M, Sahin H, Huseyin E. New platelet indices as inflammatory parameters for patients with rheumatoid arthritis. European journal of rheumatology 2014; 1:144-6.
20. Grzanka A, Machura E, Mazur B, et al. Relationship between vitamin D status and the inflammatory state in patients with chronic spontaneous urticaria. Journal of inflammation 2014; 11:2.
21. Kasperska-Zajac A. Acute-phase response in chronic urticaria. Journal of the European Academy of Dermatology and Venereology : JEADV 2012;26:665-72.
22. Jung J, Lee H, Yun T, et al. Prognostic role of the neutrophil-to-lymphocyte ratio in patients with primary central nervous system lymphoma. Oncotarget 2017;8:74975-86.
23. Balde AI, Fang S, He L, et al. Propensity score analysis of recurrence for neutrophil-to-lymphocyte ratio in colorectal cancer. The Journal of surgical research 2017;219:244-52.
24. Liu S, Zheng H, Zhu X, et al. Neutrophil-to-lymphocyte ratio is associated with diabetic peripheral neuropathy in type 2 diabetes patients. Diabetes research and clinical practice 2017;130:90-7.
25. Tamer F. Omalizumab does not lead to a distinct alteration in hematological parameters and complete blood count-derived inflammation biomarkers except for basophil count. Cutan Ocul Toxicol 2020;39:229-32.
26. Avci A, Avci D, Erden F, et al. Can we use the neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and mean platelet volume values for the diagnosis of anterior uveitis in patients with Behcet's disease? Therapeutics and clinical risk management 2017;13:881-6.
27. Özer İ, Balevi Ş, Ataseven A. Can Neutrophil/Lymphocyte Ratio Be Used As a Marker in the Diagnosis of Bullous Pemphigoid? Selcuk Med J 2018;34: 65-9.
28. Emiroglu N, Cengiz FP, Bahali AG, et al. Red Blood Cell Distribution Width and Neutrophil-to-Lymphocyte Ratio in Patients with Cutaneous Vasculitis. Annals of clinical and laboratory science 2017;47:162-5.
29. Takahagi S, Mihara S, Iwamoto K, et al. Coagulation/fibrinolysis and inflammation markers are associated with disease activity in patients with chronic urticaria. Allergy 2010;65:649-56.
30. Asero R, Tedeschi A, Riboldi P, et al. Severe chronic urticaria is associated with elevated plasma levels of D-dimer. Allergy 2008;63176-80.
31. Asero R, Tedeschi A, Riboldi P, et al. Plasma of patients with chronic urticaria shows signs of thrombin generation, and its intradermal injection causes wheal-and-flare reactions much more frequently than autologous serum. The Journal of allergy and clinical immunology 2006;117:1113-7.
32. Vena GA, Cassano N, Marzano AV, et al. The Role of Platelets in Chronic Urticaria. International archives of allergy and immunology 2016;169:71-9.
33. Isiksacan N, Koser M, Cemsitoglu F, et al. Platelet and Other Hemostatic Characteristics in Patients With Chronic Urticaria. Angiology 2014;66:387-91.
34. Kridin K, Shihade W, Zelber-Sagi S. Mean Platelet Volume in Pemphigus Vulgaris. Angiology 2017:3319717718329.
35. Kim DS, Lee J, Kim SH, et al. Mean platelet volume is elevated in patients with psoriasis vulgaris. Yonsei medical journal 2015;56:712-8.
36. Coban E, Adanir H. Platelet activation in patients with Familial Mediterranean Fever. Platelets 2008;19:405-8.
37. Yazici S, Yazici M, Erer B, et al. The platelet indices in patients with rheumatoid arthritis: mean platelet volume reflects disease activity. Platelets 2010;21:122-5.
38. Wodarczyk M, Kasprzyk J, Sobolewska-Wodarczyk A, et al. Mean

platelet volume as a possible biomarker of tumor progression in rectal cancer. Cancer biomarkers: section A of Disease markers 2016;17:411-17.
39. Akelma AZ, Mete E, Cizmeci MN, et al. The role of mean platelet volume as an inflammatory marker in children with chronic spontaneous urticaria. Allergologia et immunopathologia 2015;43:10-3.
40. Kasperska-Zajac A, Grzanka A, Jarzab J, et al. The association between platelet count and acute phase response in chronic spontaneous urticaria. BioMed research international 2014;2014:650913.
41. Chandrashekar L, Rajappa M, Sundar I, et al. Platelet activation in chronic urticaria and its correlation with disease severity. Platelets 2014;25:162-5.
42. Magen E, Mishal J, Zeldin Y, et al. Increased mean platelet volume and C-reactive protein levels in patients with chronic urticaria with a positive autologous serum skin test. The American journal of the medical sciences 2010; 339:504-8.
43. Yalcin AD, Celik B, Gumuslu S. D-dimer levels decreased in severe allergic asthma and chronic urticaria patients with the omalizumab treatment. Expert opinion on biological therapy 2014;14:283-6.
44. Metz M, Staubach P, Bauer A, et al. Clinical efficacy of omalizumab in chronic spontaneous urticaria is associated with a reduction of FcepsilonRI-positive cells in the skin. Theranostics 2017;7:1266-76.
45. Ertas R, Ozyurt K, Atasoy M, et al. The clinical response to omalizumab in chronic spontaneous urticaria patients is linked to and predicted by IgE levels and their change. Allergy 2018;73:705-12.