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Evaluation of Hematological and Inflammatory Biomarkers in Patients Receiving Omalizumab Treatment in Chronic Urticaria

Kronik Ürtikerde Omalizumab Tedavisi Alan Hastalarda Hematolojik ve İnflamatuar Biyobelirteçlerin Değerlendirilmesi

Esra İNAN DOĞAN[a], Akın AKTAŞ[b]

[a]Department of Dermatology, Adıyaman University Faculty of Medicine, Adıyaman, TURKEY
[b]Department of Dermatology, Ankara Yıldırım Beyazıt University Faculty of Medicine, Ankara, TURKEY

ABSTRACT Objective: This study aims to evaluate the effects of omalizumab on hematological parameters and inflammation biomarkers in patients diagnosed with chronic spontaneous urticaria (CSU). **Material and Methods:** The records of 109 (76 women and 33 men) patients, who were treated with omalizumab with the diagnosis of CSU were retrospectively examined. In addition, the pre-treatment and post-omalizumab treatment periods were evaluated in CSU patients by comparing hematological, inflammatory and biochemical parameters. The data of these patients were compared to a healthy control group with similar characteristics such as age and gender. **Results:** C-reactive protein (CRP), neutrophil (NEU), and monocyte values were significantly higher in patients with CSU, while basophil values in control individuals. The comparison of the measurements of the patients before and after omalizumab treatment revealed a significant reduction in CRP, white blood cell (WBC), NEU, and platelet (PLT) levels. WBC, NEU, and eosinophil levels were found to be significantly reduced in responders compared to non-responders to treatment. **Conclusion:** The evaluation of CRP, NEU, PLT levels are found to be important to show the activity of the disease in CSU. We think that these inflammatory markers are important in the follow-up of CSU and omalizumab treatment. We think that these inflammatory markers are important in the follow-up of CSU and omalizumab treatment. Our results will contribute to the medical literature to establish both the mechanism of action of omalizumab and the parameters used in the follow-up of omalizumab therapy in patients with CSU.

Keywords: Omalizumab; chronic urticaria; inflammation

ÖZET Amaç: Bu çalışmada, kronik spontan ürtiker (KSÜ) tanılı hastalarda omalizumabın hematolojik parametreler ve inflamasyon biyobelirteçleri üzerine olan etkilerinin değerlendirmesi amaçlanmaktadır. **Gereç ve Yöntemler:** KSÜ tanısıyla omalizumab ile tedavi edilmiş 109 (76 kadın, 33 erkek) hastanın hastane kayıtları retrospektif olarak incelendi. Ayrıca hastalarda tedavi öncesi ve omalizumab tedavisi sonrası dönemde hematolojik, inflamatuar ve biyokimyasal parametreler karşılaştırılarak değerlendirildi. Bu hastaların verileri yaş ve cinsiyet gibi benzer özelliklere sahip sağlıklı kontrol grubu ile karşılaştırıldı. **Bulgular:** C-reaktif protein (CRP), nötrofil (NEU), monosit değerleri KSÜ'lü hastalarda ve bazofil değeri ise kontrol bireylerinde anlamlı düzeyde daha yüksek olduğu görüldü. Hastalarda omalizumab tedavisi öncesi ve sonrası ölçümleri karşılaştırıldığında CRP, beyaz kan hücresi [white blood cell (WBC)], NEU ve platelet (PLT) düzeylerinde anlamlı azalma tespit edildi. Tedaviye yanıt veren hastalarda WBC, NEU, EOS düzeyleri, yanıt vermeyenlerle karşılaştırıldığında anlamlı düzeyde azaldığı bulundu. **Sonuç:** KSÜ'de hastalığın aktivitesini göstermek için CRP, NEU, PLT düzeylerinin değerlendirilmesinin önemli olduğu bulundu. KSÜ ve omalizumab tedavisinin takibinde bu inflamatuar belirteçlerinin önemli olduğunu düşünmekteyiz. Sonuçlarımız, KSÜ hastalarında hem omalizumabın etki mekanizmasını hem de omalizumab tedavisinde takipte kullanılan parametreleri oluşturmak için tıbbi literatüre katkıda bulunacaktır.

Anahtar Kelimeler: Omalizumab; kronik ürtiker; inflamasyon

Correspondence: Esra İNAN DOĞAN
Department of Dermatology, Adıyaman University Faculty of Medicine, Adıyaman, TURKEY/TÜRKİYE
E-mail: esranander @yahoo.com

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Urticaria is a common dermatological disease that manifests with erythematous lesions, swelling, and angioedema.[1] Chronic spontaneous urticaria (CSU), on the other hand, is a type of urticaria observed in approximately 1-2% of the population that manifests with continuous and recurrent urticaria attacks for at least 6 weeks.[2] The pathophysiology of chronic urticaria has still not been fully understood. Studies show that mast cells, basophils (BASO), and hormones play a role together with the changes in the coagulation and fibrinolysis pathway.[3-5]

Current European Academy of Allergology and Clinical Immunology Dermatology Section and the European Union (EU)-funded network advise second-generation H_1-antihistamines to control chronic urticaria symptoms. If there is no response to treatment, omalizumab treatment is given as a third line treatment.[6] Omalizumab which is a humanized monoclonal anti-immunoglobulin E (IgE) antibody acts by reducing the FcεRI receptors in BASO and mast cells and the level of free IgE.[7-9]

Omalizumab is effective in 70-80% of patients with CSU, but we don't know how omalizumab acts in CSU. Omalizumab can be effective on the decrease of inflammatory cytokines and various proteins including C-reactive protein (CRP) by stimulating IgE receptors on mast cells and BASOs.[10] Recently, there have been many studies investigating omalizumab-related hematological parameters such as CRP, eosinophil (EOS), BASO, monocyte (MONO) and platelet/lymphocyte ratio (PLR), and neutrophil/ platelet ratios (NPR) but there is still no full consensus on the matter.[11-13] CRP is a sensitive biomarker of inflammation, and the correlation of disease activity with CRP has been reported previously in patients with CSU.[12]

In particular, mean platelet volume (MPV) is a sign of platelet (PLT) reactivity and an indicator of inflammation and is also involved in the pathogenesis of inflammation and coagulation activation.[6,14-16] An elevation and reduction in MPV during inflammation can lead to changes in PLT count and volume. Increased MPV and CRP have been implicated in chronic inflammatory diseases such as CSU, rheumatoid arthritis, familial Mediterranean fever, and cystic fibrosis.[2]

Neutrophil/lymphocyte ratio (NLR) has been considered as an important marker of inflammation in chronic diseases.[17,18] Similarly, PLR is an important inflammation indicator like NLR.[19,20] There are also studies indicating that CRP is a prognostic marker showing disease activity.[21]

In our research, we investigated activity of omalizumab on hematological and inflammatory values in chronic urticaria. Our findings will guide the literature on the mechanism of action of omalizumab and the parameters used in omalizumab therapy in the follow-up of patients with chronic urticaria.

MATERIAL AND METHODS

Local ethics committee approval was obtained from Adıyaman University Non-interventional Clinical Researches Ethics Committee (approval number: 2020/6-57 date: 23.06.2020) prior to the study. Our study was carried out in accordance with the Declaration of Helsinki Principles. In our study, 109 patients, 76 women and 33 men, over the age of 18, who were treated with omalizumab administered subcutaneously at a monthly dose of 300 mg in our dermatology clinic between the years of 2016 and 2020, were retrospectively evaluated. The patients did not use any other drugs used in the treatment of urticaria such as antihistamine drugs, doxepin, cyclosporine, and corticosteroids other than omalizumab. Patients who were followed up for chronic urticaria used oral antihistamine treatments for 6 months. These treatments were discontinued 15 days before starting omalizumab treatment. Findings of the patients, as well as the values before starting omalizumab treatment and at 3 months of omalizumab treatment, were evaluated. Hematological parameters, as well as inflammation biomarkers including NLR and PLR, were analyzed.[22] NLR shows the ratio of neutrophil (NEU) to lymphocyte (LYM) and PLR shows the ratio of PLT to LYM.

Patients with an active infection, infectious disease, liver disease, kidney disease, malignancy, and hematological disease, those who received immunosuppressive therapy, those who took iron-containing drugs that affect PLT function, and those who used other drugs other than omalizumab for the treatment of urticaria were excluded from the study.

Complete blood count (CBC) parameters, red cell distribution width (RDW), MPV and CRP levels, aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), and creatinine values before starting treatment and after third month of treatment were retrospectively analyzed. Response rates of the patients were calculated according to the urticaria activity score (UAS). Those with UAS values greater than seven were considered as non-responsive to treatment. Values of seven and below indicated the presence of a response to treatment.

STATISTICAL ANALYSIS

Descriptive statistics of the obtained data were calculated as mean±standard deviation (SD), quartiles (25^{th}, median and 75^{th}), number and percentage frequencies depending on the type of features. Compliance of numerical type features to normal distribution was examined by the Kolmohorov-Smirnov test. Mann-Whitney U test was used to compare patient and control groups in terms of numerical type characteristics. Besides, the Mann-Whitney U test was used to compare responders and non-responders to treatment, in terms of blood parameters measured at baseline and at month 3 and in terms of changes in these blood parameters. The significance of the change occurring between the blood parameters measured at baseline and at month 3 in the patient group was examined by the Wilcoxon Sign Rank test. Relationships between the duration of urticaria and blood parameters measured at baseline and month 3 were analyzed using Spearman rank correlation analysis. The gender distribution of the groups was evaluated using Pearson's chi-square analysis. $p<0.05$ was considered as the statistical significance level and the SPSS (ver. 23) software was used in calculations.

RESULTS

One hundred and nine patients with CSU, 76 (69.7%) females and 33 (30.3%) males, were included in the study. The mean age of the patients was 44.03±14.64 years (distribution: 18 to 79 years). The average disease time was 15.8±6.2 months (distribution: 6-35 months). The control group consisted of 48 healthy individuals, 34 (70.8%) females and 14 (29.2%) males. The mean age of the control group was 43.19±10.07 years (distribution: 23 to 60 years). There was no significant difference in gender distribution between the two groups ($p>0.05$). There was no significant difference between the control group and the patient group in terms of mean age ($p>0.05$) In addition, mean CRP, mean NEU and mean MONO were found to be significantly higher in patients and mean BASO higher in control subjects. ($p<0.05$) Apart from this, there was no significant difference between the two groups in WBC, hemoglobin (HGB), hematocrit (HTC), MPV, RDW, LYM, PLT and EOS. Descriptive statistics of numerical type characteristics measured from control and diseased individuals were given in Table 1.

Upon comparison of the measurements of the patients before the treatment and at month 3 after omalizumab treatment, it was observed that there were significant changes in CRP, WBC, NEU and PLT ($p<0.05$). According to these results, it was determined that the mean CRP, WBC, NEU and PLT reduced significantly at month 3. Apart from that, there was no significant difference between baseline and third month in terms of mean HGB, HCT, MPV, RDW, LYM, MONO, EOS, BASO, NLR, PLR, AST, ALT, BUN and CRE ($p>0.05$) (Table 2).

Table 3 demonstrates the comparative results of the blood parameters of the responders and non-responders to treatment at baseline and at the end of the third month. The examination of Table 3 revealed that the mean of EOS was significantly higher in responders ($p<0.05$). Mean of WBC at third month was significantly lower in responders ($p<0.05$). The mean of LYM at third month was significantly lower in responders ($p<0.05$). The mean of AST at third month was significantly lower in responders ($p=0.046$), and the mean of CRE at third month was found to be significantly lower in responders. ($p<0.05$) In terms of other measurements in Table 3, there was no significant difference between responders and non-responders ($p>0.05$).

The relationships between the duration of urticaria and blood parameters measured at baseline and third month are shown in Table 4. Examination of Table 4 revealed that there was a significant positive

TABLE 1: Descriptive statistics of numerical type characteristics measured from control and diseased individuals.

	Control						Patients (pre-treatment)						
				Percentiles						Percentiles			
	N	Mean	SD	25	Median	75	N	Mean	SD	25	Median	75	p value*
Age	48	43.19	10.07	34.25	44.00	52.00	109	44.03	14.64	34.00	44.00	54.00	0.864
CRP	48	0.14	0.06	0.10	0.13	0.19	109	1.55	1.16	0.42	1.40	2.42	0.001
WBC	48	8.17	1.77	6.77	7.82	9.24	109	8.99	2.91	7.31	8.47	10.34	0.150
HGB	48	13.98	1.75	12.62	13.67	15.36	109	14.00	1.84	12.90	14.10	15.15	0.705
HTC	48	42.91	4.66	40.25	41.80	46.74	109	42.28	4.52	39.50	42.40	45.05	0.602
MPV	48	7.77	1.32	6.77	7.74	8.91	109	7.97	1.43	6.90	7.59	8.78	0.648
RDW	48	12.17	1.26	11.45	12.01	12.87	109	12.49	1.62	11.30	12.10	13.41	0.412
NEU	48	4.63	1.39	3.65	4.41	5.38	109	5.66	2.70	3.78	4.78	6.96	0.041
LYM	48	2.68	0.72	2.10	2.61	3.13	109	2.48	0.83	2.01	2.39	2.94	0.161
PLT	48	267.34	55.79	231.00	264.30	296.80	109	258.33	63.79	212.50	248.00	296.00	0.194
MONO	48	0.47	0.15	0.35	0.44	0.56	109	0.57	0.24	0.38	0.54	0.72	0.012
EOS	48	0.15	0.11	0.07	0.12	0.19	109	0.19	0.15	0.09	0.16	0.27	0.123
BASO	48	0.09	0.08	0.06	0.08	0.09	109	0.07	0.06	0.05	0.06	0.09	0.019
NLR	48	1.82	0.66	1.21	1.71	2.23	109	2.63	2.07	1.53	2.04	2.74	0.01
PLR	48	106.2	37.1	82.39	97.8	120.8	109	122.29	108.37	85.95	101.35	132.43	0.41

*Mann-Whitney U test; p≤0.05; SD: Standard deviation; CRP: C-reactive protein; WBC: White blood cell; HGB: Hemoglobin; HTC: Hematocrit; MPV: Mean platelet volume; RDW: Red cell distribution width; NEU: Neutrophil; LYM: Lymphocyte; PLT: Platelet; MONO: Monocyte; EOS: Eosinophil; BASO: Basophil; NLR: Neutrophil/lymphocyte ratio; PLR: Platelet/lymphocyte ratio.

TABLE 2: Changes in blood values before and after omalizumab treatment.

	Pre-treatment					Post-treatment					
			Percentiles					Percentiles			
	Mean	SD	25	50	75	Mean	SD	25	Median	75	p value
CRP	1.55	1.16	0.42	1.40	2.42	0.73	0.60	0.29	0.60	0.90	<0.001
WBC	8.99	2.91	7.31	8.47	10.34	8.16	2.11	6.65	7.85	9.40	0.015
HGB	14.00	1.84	12.90	14.10	15.15	13.99	1.69	12.90	13.90	15.15	0.382
HTC	42.28	4.52	39.50	42.40	45.05	42.60	4.30	39.57	42.50	45.60	0.624
MPV	7.97	1.43	6.90	7.59	8.78	8.21	1.38	7.28	7.95	8.87	0.147
RDW	12.49	1.62	11.30	12.10	13.41	12.60	1.83	11.35	12.17	13.20	0.515
NEU	5.66	2.70	3.78	4.78	6.96	4.89	1.76	3.58	4.44	5.96	0.016
LYM	2.48	0.83	2.01	2.39	2.94	2.46	0.77	1.93	2.39	2.83	0.360
PLT	258.3	63.8	212.5	248.0	296.0	248.6	62.4	208.0	234.0	282.5	0.020
MONO	0.57	0.24	0.38	0.54	0.72	0.53	0.22	0.38	0.50	0.69	0.232
EOS	0.19	0.15	0.09	0.16	0.27	0.20	0.20	0.08	0.14	0.26	0.962
BASO	0.07	0.06	0.05	0.06	0.09	0.08	0.05	0.05	0.07	0.10	0.220
NLR	2.63	2.07	1.53	2.04	2.74	2.25	1.88	1.52	1.82	2.55	0.086
PLR	122.29	108.37	85.95	101.35	132.43	110.73	45.93	81.23	101.74	131.17	0.982
AST	18.95	8.23	14.00	17.00	21.50	19.31	7.21	15.00	18.00	22.00	0.580
ALT	20.53	12.91	13.00	18.00	24.00	21.98	12.94	13.00	20.00	26.00	0.289
BUN	26.13	8.10	20.00	25.00	32.00	25.94	8.82	20.00	25.00	30.00	0.967
CRE	0.74	0.11	0.66	0.72	0.80	0.76	0.15	0.68	0.73	0.83	0.114

*Wilcoxon sign test; p≤0.05; SD: Standard deviation; CRP: C-reactive protein; WBC: White blood cell; HGB: Hemoglobin; HTC: Hematocrit; MPV: Mean platelet volume; RDW: Red cell distribution width; NEU: Neutrophil; LYM: Lymphocyte; PLT: Platelet; MONO: Monocyte; EOS: Eosinophil; BASO: Basophil; NLR: Neutrophil/lymphocyte ratio; PLR: Platelet/lymphocyte ratio; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; BUN: Blood urea nitrogen.

TABLE 3: Comparative results of responders and non-responders.

	No Response						Response						
	N	Mean	SD	25th	Median	75th	N	Mean	SD	25th	Median	75th	p value
CRP	16	0.86	0.78	0.29	0.70	0.91	93	0.71	0.56	0.29	0.56	0.90	0.607
WBC	16	9.19	2.48	7.35	9.19	10.39	93	7.99	2.00	6.58	7.62	9.07	0.049
HGB	16	13.49	2.32	12.41	14.25	14.95	93	14.08	1.55	12.96	13.90	15.20	0.555
HTC	16	41.56	6.25	38.90	42.10	45.30	93	42.78	3.88	39.65	42.50	46.00	0.572
MPV	16	8.70	1.53	7.63	8.75	9.41	93	8.13	1.34	7.24	7.82	8.71	0.061
RDW	16	13.75	3.03	11.33	12.55	15.55	93	12.40	1.48	11.35	12.10	13.10	0.205
NEU	16	5.54	2.00	3.81	5.55	6.53	93	4.78	1.70	3.52	4.40	5.71	0.141
LYM	16	2.89	0.93	2.34	2.82	3.24	93	2.39	0.72	1.91	2.30	2.70	0.021
PLT	16	253.56	71.23	201.00	238.00	311.25	93	247.81	61.11	208.00	234.00	281.00	0.817
MONO	16	0.55	0.22	0.47	0.54	0.61	93	0.53	0.22	0.37	0.50	0.70	0.604
EOS	16	0.17	0.29	0.05	0.10	0.19	93	0.20	0.18	0.10	0.16	0.27	0.038
BASO	16	0.08	0.03	0.05	0.08	0.10	93	0.08	0.05	0.05	0.07	0.09	0.618
NLR	16	2.04	0.81	1.43	2.00	2.58	93	2.29	2.01	1.52	1.78	2.55	0.966
PLR	16	97.52	48.13	65.56	88.49	102.95	93	113.00	45.42	82.01	102.75	136.56	0.078
URTICARIA DURATION	16	12.94	5.42	8.00	12.00	17.50	93	17.13	6.88	12.00	15.00	23.00	0.732

CRP: C-reactive protein; WBC: White blood cell; HGB: Hemoglobin; HTC: Hematocrit; MPV: Mean platelet volume; RDW: Red cell distribution width; NEU: Neutrophil; LYM: Lymphocyte; PLT: Platelet; MONO: Monocyte; EOS: Eosinophil; BASO: Basophil; NLR: Neutrophil/lymphocyte ratio; PLR: Platelet/lymphocyte ratio.

correlation between the measurements of EOS and WBC at third month. As the duration of urticaria prolonged, the values of EOS and WBC at third month also increased (p values 0.038 and 0.049). However, it was determined that the prolongation in the duration of urticaria did not have a significant linear relationship with other parameters.

TABLE 4: Relationships between the duration of urticaria in patients and blood parameters measured at end of the third month.

	Urticaria_Duration_Month		
	Spearman's R	p value	N
CRP	0.074	0.445	109
WBC	0.050	0.604	109
HGB	0.060	0.533	109
HTC	0.057	0.555	109
MPV	0.032	0.742	109
RDW	0.087	0.371	109
NEU	0.128	0.185	109
LYM	-0.103	0.286	109
PLT	-0.051	0.601	109
MONO	-0.008	0.932	109
EOS	0.205	0.033	109
BASO	-0.073	0.450	109
NLR	0.189	0.049	109
PLR	0.069	0.474	109

CRP: C-reactive protein; WBC: White blood cell; HGB: Hemoglobin; HTC: Hematocrit; MPV: Mean platelet volume; RDW: Red cell distribution width; NEU: Neutrophil; LYM: Lymphocyte; PLT: Platelet; MONO: Monocyte; EOS: Eosinophil; BASO: Basophil; NLR: Neutrophil/lymphocyte ratio; PLR: Platelet/lymphocyte ratio.

DISCUSSION

Acute and chronic infections, hypersensitivity reactions to foods and drugs, idiopathic causes, autoimmunity are the most common factors in the etiology of CSU. Mast cell activation and proinflammatory cytokine secretions are involved in the development of urticaria.[1,23]

In CSU, omalizumab which is a monoclonal antibody, prevents the development of angioedema, improves the quality of life, and is recommended as an appropriate therapy for long-term use.[24] However, since physiopatology in CSU is unknown yet, it is thought there was multiple mechanisms.

Although function of BASOs in the physiopatology of CSU is not known yet, BASO accumulation in skin lesions has been indicated in the disease.[25] This can be explained by the significantly low BASO level in peripheral blood in CSU.[26] Besides, omalizumab can prevent the migration of histamine to chemokine receptors in BASOs.[25] The BASO count was found to be statistically significantly hıgher in

the control group compared to patients with CSU. We think that this is due to the migration of BASOs in the peripheral blood to the area where urticaria lesions are present.[27] Moreover, inflammatory markers such as BASO count, PLT count, CRP, and MPV may be associated with disease severity.[15,21,28]

Omalizumab can show its anti-inflammatory effect in patients with CSU by decreasing inflammatory markers in the serum and changing hematological parameters. In our study, the CRP level was found to be statistically significantly higher in the control group than in the patient group. In patients with CSU, the CRP level was found to be higher than in the control group, as in inflammatory diseases such as rheumatoid arthritis, Behçet's disease, and familial Mediterranean fever.[29] The CRP level before omalizumab treatment was found to be statistically significantly higher than the CRP level at the end of the 3rd month, as in the study conducted by Akdogan et al.[29,30] As in our study, there are studies showing the anti-inflammatory effect of omalizumab by lowering the CRP level in patients with CSU.[29,30] There are many studies in which this inflammatory parameter is used to evaluate the activity, severity, and response of the disease.[31,32] As in our study, the significant reduction in CRP levels after omalizumab treatment shows that omalizumab treatment has an anti-inflammatory effect.[29]

A positive correlation was found between CRP levels and UAS.[31] In our study, the CRP level in patients with UAS <7 was found to be lower than in patients with UAS >7. However, the findings were not statistically significant.

In addition, there are opinions that in CSU pathogenesis, EOSs facilitate the increase in vascular permeability and provide vascular endothelial growth factors.[33] Although omalizumab is effective through reducing serum total EOS count in CSU in relation to EOS apoptosis, the results of the studies differ. One study concluded that the use of omalizumab did not change the EOS count.[34] However, studies conducted in recent years have found an elevation in the number of EOSs due to the use of omalizumab.[29,30] Similar to the studies in current years, an elevation in the number of EOSs was found due to the use of omalizumab in our study, but this high value was not statistically significant. In addition, a statistically significant elevation in the number of EOSs was detected in responders and with prolonged urticaria duration. No statistically significant difference was found between the control group and CSU group in terms of WBC, HGB, HTC, MPV, RDW, NEU, LYM, PLT, MONO, BAZO, and PLR. However, the NLR value was found to be statistically significantly higher in the patient group compared to the control group.

In the study published by Acer et al., a statistically significant reduction was found in CRP, WBC, NEU, and PLT levels when compared pre- and post-omalizumab treatment.[30] The reduction in these values at the end of the treatment indicates that it may be related to the severity of the disease.[15,21,28] Since omalizumab has an anti-inflammatory effect, it can reduce the levels of inflammation markers in the serum of patients with CSU.[35] In addition, many studies have shown that omalizumab prevents inflammation by changing hematological parameters.[15,21,28]

A reduction was detected in NLR and PLR values after treatment. Acer et al. showed a significant reduction in NLR value after third months of omalizumab treatment.[30] On the other hand, Ertaş et al. found a reduction in NLR and PLR values and an elevation in MPV, as in our case.[35] However, this reduction was not found to be statistically significant as in our study.

PLTs play an important role in CSU pathogenesis. MPV is a marker that specifically measures PLT size and also indicates PLT reactivity. Studies have shown that increased MPV level indicates an active inflammatory response.[19,20] MPV is used as an inflammatory marker in many diseases mediated by inflammation, as in CSU. Many studies found that MPV increased, decreased, or showed no change in CSU.[9,15] Ertaş et al. detected an elevation in MPV level after three month treatment and thought that this effect might be related to the block of megakaryopoiesis.[35] Similar to current studies, we found an elevation in MPV level, but this elevation was not statistically significant.

The significant reduction in NEU and PLT counts after omalizumab treatment was not at a level

to cause neutropenia or thrombocytopenia in any patient. In conclusion, close monitoring of hematological parameters is not required in patients receiving omalizumab treatment. In addition, there is no difference in the values of AST, ALT, BUN and creatinine before and after omalizumab treatment. This shows us that it is not necessary to follow up on liver and kidney function tests for 3 months. Based on this knowledge, when we investigated the impact of omalizumab on hematological values, a significant reduction was found in CRP, NEU, PLT, WBC values at the end of month 3. However, the reduction in NLR and PLR values was not statistically significant, such a reduction was also reported in previous studies.[30,34,35] Our results show that omalizumab treatment in CSU has a decreasing effect on inflammation markers such as CRP and PLTs.

The limitations of our research are that it was designed retrospectively and there was no histopathological examination to compare these results with blood counts. Since the study was conducted in a single-center, the findings of the research should not be generalized to the world people. Since the results of the study were limited to a period of three months, it is not known how the values will change further in the omalizumab treatment later on.

CONCLUSION

In conclusion, although omalizumab has an effect of inducing a significant reduction in CRP, PLT levels, which are inflammatory markers, and WBC, NEU levels, which are hematological parameters, in patients with CSU, it has no effect of inducing any change on other hematological and biochemical parameters. It has been found that it is important to evaluate the CRP, NEU, PLT levels to show the activity of the disease in CSU. We think that these inflammatory markers are important in the follow-up of CSU and omalizumab treatment.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Esra İnan Doğan;* ***Design:*** *Esra İnan Doğan;****Control/Supervision:*** *Akın Aktaş;* ***Data Collection and/or Processing:*** *Esra İnan Doğan;* ***Analysis and/or Interpretation:*** *Akın Aktaş;* ***Literature Review:*** *Esra İnan Doğan;* ***Writing the Article:*** *Esra İnan Doğan;* ***Critical Review:*** *Akın Aktaş;* ***References and Fundings:*** *Esra İnan Doğan;* ***Materials:****Esra İnan Doğan.*

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