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EFFECTS OF İNFLİXİMAB TREATMENT ON İNFLAMMATORY MARKERS İN THE TREATMENT OF RESİSTANT PSORİASİS

General Surgery

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ABSTRACT

Objective: To investigate the changes in neutrophil / lymphocyte ratio and mean platelet volume levels, which are inflammatory markers, by treatment with infliximab in chronic resistant psoriasis patients treated with infliximab.

Patients and methods: The study was conducted with a total of 110 patients, including 50 patients with refractory psoriasis using infliximab and 60 healthy volunteers. Neutrophil lymphocyte ratio (NLR) and mean platelet volumes (MPV) of patients were calculated at the beginning of treatment. Infliximab was administered every 8 weeks after administration at 5 mg / kg doses at 0, 2, 6 and 14 weeks. At 12 months, blood samples were taken again for MPV and NLR levels.

Findings: Median NLR value before infliximab treatment was 2.32 (1.20-16.37). The median NLR at week 12 was 2.02 (1.0-6.88). There was a statistically significant difference between the two values ($p = 0.048$). The mean MPV values of the group of healthy volunteers were 9.85 ± 1.35 fL. The difference was statistically significant ($p = 0.002$) when the mean value of MPV before treatment was compared with that of patients with psoriasis, which was 9.0 ± 1.56 fL.

Conclusion: With infliximab therapy, inflammation is suppressed in psoriasis, an inflammatory disease, which is also reflected in inflammatory markers such as NLR and MPV.

KEYWORDS

Psoriasis, infliximab, inflammation, neutrophil lymphocyte ratio, MPV

INTRODUCTION

Psoriasis is a chronic, inflammatory and immun-mediated skin disorder that can be associated with multisystem comorbidities. Biological treatments may become an option if methotrexate, cyclosporin, acetyltretin or phototherapy (PUVA, narrow band UVB) is unresponsive in moderate and severe psoriasis treatment (1, 2). Infliksimab is a chimeric anti-tumor necrosis factor agent used in chronic plaque psoriasis, psoriatic arthritis, psoriatic erythroderma and pustular psoriasis, and was first approved in 2010 for the treatment of psoriasis (3). After application at 5 mg / kg intravenously at 0, 2, 6 and 14 weeks, application is continued every 8 weeks. Efficacy of the agent may decrease over time in the coming weeks (4, 5, 6).

Mean platelet volume (MPV) and neutrophil lymphocyte ratio (NLO) are used as indicators of inflammation in many inflammatory diseases (7, 8). The aim of this study is to show whether patients with initial inflammatory markers (NLR and MPV) have changed with 12-month infliximab therapy in psoriasis, an inflammatory disease.

PATIENTS AND METHODS

Patient and healthy volunteer group consisted of 50 patients (resistant to the classic psoriasis treatments) and 60 healthy volunteers who applied to Training and Research Hospital, Department of Dermatology and used infliximab for resistant psoriasis. Patients with moderate to severe psoriasis infliximab were given every 8 weeks after administration in the hospital setting at doses of 5 mg / kg at 0, 2, 6 and 14 weeks and blood samples were taken again for MPV and NLR levels at 12th month. MPV and NLR values were recorded. The values at the beginning and 12th month were statistically compared. MPV and NLR values were also recorded in the healthy volunteer group. The NLR was calculated based on the ratio of the absolute value of neutrophil to the absolute value of lymphocyte. Patients previously using any biological agent (adalimumab, etanercept, ustekinumab, etc.) were excluded from the study.

Statistical analysis

Whether the distributions of the data were normal or not was determined using histograms and the Shapiro-Wilk test. Continuous variables were presented as mean ± standard deviation or median (minimum-maximum), depending on whether their distribution is normal or not. The mean values between the groups were compared using Student's T test, and the mean values were compared using the Mann-Whitney-U test. Chi-square test was used to compare categorical data. Pearson correlation analysis was used for the correlation calculations between continuous variables. A value of p <0.005 was considered statistically significant. All statistical analyzes were performed using Statistical Package for the Social Sciences (SPSS), version 21.0 (SPSS Inc., Chicago, IL, US).

According to the Helsinki Declaration of 2004, the necessary approvals were obtained from the local ethics committee.

RESULTS

The study was carried out with 110 patients consisting of 60 healthy volunteers and 50 patients with resistant psoriasis.

The mean age of the patients in the psoriasis group was 45.0 ± 12.4 years. The mean age in the control group was 43.6 ± 15.8 years. There was no statistically significant difference between the average of the two groups ($p = 0.616$).

Of the patients in the psoriasis group, 58.0% (n = 18) were male and 42.0% (n = 14) were female. In the control group, 56.7% of the volunteers were male (n = 34) and 43.3% (n = 26) were female. The two groups were similar in terms of gender ($p = 0.969$).

The baseline CRP values of the patients were 3.65 (2.97-80.7) mg / dL, while the values after 12 months were 4.37 (1.20-16.37) mg / dL. CRP values at baseline and 12th month did not differ statistically ($p = 0.588$).

The median NLR value in the control group was 1.94 (0.73-6.50). This is lower than the patient's untreated value of 2.32 (1.20-16.37). The difference between the median NLR values between the two groups was statistically significant ($p = 0.018$).

Median NLR value of the patients before treatment was 2.32 (1.20-16.37). The NLR at week 12 was 2.02 (1.0-6.88). There was a statistically significant difference between the two values ($p = 0.048$).

When the median NLR value of 2.02 (1.0-6.88) after 12 weeks of treatment and the median value of healthy volunteers 1,94 (0.73-6.50) were compared, the difference was not significant ($p = 0.585$). In other words, the NLR value could be reduced to the level of normal volunteers by treatment with infliximab.

The mean MPV values of the group of healthy volunteers were 9.85 ± 1.35 fL. When the mean MPV of healthy volunteers was compared with the pre-treatment mean MPV of 9.0 ± 1.56 fL in patients with psoriasis, the difference was statistically significant ($p = 0.002$).

The median MPV of the patients was 9.0 ± 1.56 fL before the medication and $10.10 \pm 1,16$ fL at 12 weeks after the use of infliximab.

This change in MPV value was statistically significant (p <0.001).

There was no statistically significant difference (p = 0.301) between the mean MPV of patients 10.10 ± 1.16 fL obtained after infliximab treatment and the mean MPV of 9.85 ± 1.35 fL of healthy volunteers. In other words, the drug had reached the MPV of normal healthy volunteers.

The whole comparisons are summarized in table 1.
Table 1: Comparisons of healthy controls, pre-infliximab psoriasis patients and 12th month after initiation of treatment.

	Healty Controls	Infliximab Group Before Treatment	Infliximab Group After 12 Months	P
AGE (years)	43.6±15.8	45.0±12.4		p=0.616
CRP (mg/dL)		3.65 (2.97-80.7)	4.37 (1.20-16.37)	p=0.588
NLR (Ratio)	1.94 (0.73-6.50)[A,C]	2.32 (1.20-16.37)[A,B]	2.02 (1.0-6.88)[B,C]	p=0.048[A] p=0.018[B] p=0.585[C]
MPV (fL)	9.85±1.35[D,F]	9.0±1.56[D,E]	10.10±1.16[E,F]	p=0.002[D] p<0.001[E] p=0.301[F]

The upper symbols indicate the value of p, which is the comparison of the two parameters.

DISCUSSION

Genetic susceptibility is important in the development of this disease. The most common type is the silver colored pearl-like scales. Initially, keratinocyte dysfunction was shown as the main factor in pathogenesis, however, today, dysregulation in the immun system is the main pathogenesis. The role of inflammation in the pathogenesis of psoriasis is also predominant. Mediators that play a role in pathogenesis; dendritic cells (plasma dendritic cells, myeloid dendritic cells), macrophages and neutrophils, interferon alfa, tumor necrosis factor alpha, interleukin 17, interleukin 23, interleukin 12.

Infliximab is an expensive anti-tumor necrosis factor alpha biological agent used in the treatment of moderate to severe psoriasis (9, 10, 11). It is also used in the treatment of many autoimmune diseases such as rheumatoid arthritis, ankylosing spondylitis, Behçet's disease, Crohn's disease and ulcerative colitis (12-15). It have also been successfully used in Erythrodermic psoriasis (19, 20) and pustular psoriasis (21, 22). Tumor necrosis factor alpha is increased in patient serum as well as in active psoriasis plaques (16). The basis of the mechanism of action of infliximab is the reduction of this increased tumor necrosis factor alpha. The chemical structure is a chimeric monoclonal antibody consisting of 25% mouse and 75% human IgG1. There is a great deal of binding capacity to human tumor necrosis factor alpha in the tissue (17, 18).

Our goal in this research is to find out how the severity of inflammation changes in psoriasis with the treatment of infliximab, a biological agent. For this purpose, we examined NLR and MPV as markers of inflammation.

In our study, NLR values were significantly higher in the psoriasis group compared to the control group. NLR levels were also reduced by treatment with infliximab for 12 months. Median NLR value of the patients before treatment was 2.32 (1.20-16.37). The NLR at week 12 was 2.02 (1.0-6.88). There was a statistically significant difference between the two values.

The median MPV of the patients was 9.0 ± 1.56 fL before the medication and 10.10 ± 1.16 fL at 12 weeks after the medication. This change in MPV value was statistically significant. There was no statistically significant difference (p = 0.301) when MPV values of patients were 10.10 ± 1.16 fL after infliximab treatment and 9.85 ± 1.35 fL of healthy volunteers. In other words, the drug had reached the MPV of normal healthy volunteers.

CONCLUSSION

According to these results, it can be said that NLR and MPV measurements, which are accepted as inflammation markers, can give an idea about the degree of inflammation in psoriasis, an inflammatory disease. We did not find any other study investigating the association of

the use of infliximab with NLR and MPV values in the literature, in patients with psoriasis or other illnesses to date. The feature of this article is that it is the first work on the subject in the literature. If similar studies are done with other biological agents, we think that the subject will be better illuminated.

Conflict of interest: there is no conflict of interest to declare.

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