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Original Article

The effect of secukinumab treatment on hematological parameters in ankylosing spondylitis and psoriatic arthritis

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Abstract

Objective: Secukinumab, a new treatment agent, selectively neutralizes interleukin (IL)-17A. It is used in the treatment of ankylosing spondylitis (AS), psoriatic arthritis (PsA), and psoriasis. It is known that the agents used in the treatment of rheumatic diseases have effects on hematological parameters. In this study, we aimed to determine whether hematological parameters are affected in secukinumab therapy in patients with AS and PsA.

Methods: Thirty-six patients on secukinumab treatment were included in the study by scanning the database of our hospital. Data on patients' age, gender, complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), uric acid, aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, creatinine values, and additional drug treatments were recorded from our database. The 0- and 6-month values of patients were analyzed.

Results: Sixteen males (44.4%) and 20 females (55.6%) were included in our study. The average age was calculated to be 39.8±8.9 years. Of these, 30 patients receiving secukinumab treatment were diagnosed with AS, and 6 patients were diagnosed with PsA. Twenty-three patients (63.9%) were continued with secukinumab treatment at the 6th month. When CBC, glucose, urea, creatine, AST, ALT, ESR, CRP, and uric acid values of the patients at 0 and 6 months were compared, there was no significant difference.

Conclusion: In our study, no significant difference was found between 0 and 6 months in terms of CBC, AST, ALT, urea, creatinine, uric acid, glucose, CRP, and ESR levels in patients receiving secukinumab. However, an increase in hemoglobin values was observed in patients who continued the treatment. These results may suggest that secukinumab treatment has no negative effects on hematological parameters.

Keywords: Secukinumab, ankylosing spondylitis, psoriatic arthritis, hematological parameters

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Introduction

Spondylarthritis (SpA) group of diseases consists of ankylosing spondylitis (AS), non-radiological axial SpA (nr-axSpA), undifferentiated spondyloarthritis (USpA), reactive arthritis, psoriatic arthritis (PsA), and enteropathic arthritis. This group of diseases can have axial (spondylitis and sacroiliitis) and peripheral involvement (arthritis, dactylitis, and enthesitis). The SpA group of diseases have some common features, such as onset of the disease at a young age, development of uveitis, and human leukocyte antigen (HLA)-B27 positivity (1-3). Axial spondyloarthritis (ax-SpA) usually occurs before the age of 45 years and leads to chronic back pain due to potentially affected vertebral column. Ax-SpA is also associated with some non-articular features, including uveitis, psoriasis, and inflammatory bowel disease (IBD) (4). PsA is a heterogeneous inflammatory disease with different clinical presentations seen equally in men and women. While peripheral arthritis is observed in almost all patients diagnosed with PsA, axial involvement can only be seen in almost half of the patients (5-7).

Although there are important developments regarding this disease group, the etiology of the SpA group diseases is not exactly unknown (8). It has been shown that interleukin (IL)-23/Th17 pathway plays a role in the pathogenesis of SpA group of diseases (9). IL-17 is a cytokine with six different subtypes (IL17-A, B, C, D, E, and F) (10). IL-23 stimulates Th17 cells by polarizing naive T cells into Th17. IL-17 is produced by stimulated

Th17 cells. IL-17 increases the production of many cytokines and stimulates keratinocytes, synoviocytes, macrophages, fibroblasts, and neutrophils. The role of IL-17 pathway in the pathogenesis of diseases, such as psoriasis, PsA, and AS, has been revealed in all aspects. Today, drugs targeting IL-17 are used in the treatment of psoriasis, PsA, and AS (11, 12). Secukinumab, a new treatment agent, is a monoclonal antibody with the human-derived immunoglobulin-G1 structure that targets IL-17A (13). Secukinumab is used as a monthly subcutaneous injection after loading doses (14).

The side effect profiles of standard traditional therapies that have been used for a long time in the management of rheumatic diseases are well known. Especially, bone marrow suppression is significant side effect. However, as the pathogenesis of the disease is better understood, new therapeutic agents are being developed. Phase studies are conducted to investigate undesirable side effects while developing these treatment agents. However, clinicians remain concerned about the undesirable effects of the drug in real life. In this respect, the effect of new treatment options on hematological parameters is always a matter of curiosity. In this study, we aimed to determine whether complete blood count (CBC) and routine parameters are affected in patients diagnosed with AS and PsA who receive secukinumab therapy in real life.

Methods

A total of 36 patients who received secukinumab (Verxant, Farmanova, Novartis Pharma Stein AG, Stein, and Switzerland) therapy, 30 of whom were diagnosed with AS and 6 with PsA, and previously applied to the internal medicine rheumatology outpatient clinic of our hospital were included in our study retrospectively by scanning the database.

The data on patients' age, gender, CBC, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), uric acid, aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, and creatinine were recorded by scanning our database. Hemoglobin (Hb), hematocrit (Htc), mean erythrocyte volume (MCV), mean erythrocyte hemoglobin concentration (MCHC), mean erythrocyte distribution width (RDW), leukocyte (WBC), neutrophil, lymphocyte, platelet, mean platelet volume (MPV), and eosinophil values were recorded. The values of these parameters of patients were compared at initial and at sixth months.

Written informed consent was obtained from all patients who participated in this study. Approval was obtained from the Non-Interventional Research Ethics Committee of Fırat University for our study (Approval Date: May 29, 2020; Approval Number: 2020/08-01).

Statistical analysis

Statistical analyses were performed using the IBM Statistical Package for the Social Sciences software for Windows version 23.0 (IBM SPSS Corp.; Armonk, NY, USA). Data are expressed as mean±standard deviation. Paired samples *t*-test was performed for the analysis of dependent variables. P<0.05 was considered significant.

Main Points

- Secukinumab, targeting IL-17A, is used in the treatment of AS and PsA.
- In patients with AS and PsA treated with biological agents, adverse events on hematological parameters can be observed.
- Secukinumab therapy in patients with AS and PsA does not have any negative effects on hematological parameters.

Results

A total of 36 patients, 16 males (44.4%) and 20 females (55.6%), were included in our study. The mean age of patients was 39.8±8.9 years. Our study population consisted of 30 patients with AS and 6 patients with PsA receiving secukinumab therapy. Twenty-three patients were using non-steroidal anti-inflammatory drugs (NSAIDs) in addition to secukinumab treatment.

Twenty-three patients (63.9%) were continued with secukinumab treatment at the 6th month. Thirteen patients (36.1%) did not continue the treatment. The reasons for discontinuation secukinumab treatment were lack of efficacy in 8 patients and adverse events in 3 patients. The adverse events observed in these patients were urticaria in 2 patients and IBD in 1 patient. Treatment of 2 patients was discontinued because they did not continue their follow-up.

There was no significant difference between the CBC, glucose, urea, creatine, AST, ALT, ESR, CRP, and uric acid values of the patients at 0 and 6 months (Table 1). When 0 and 6 months of treatment were compared, Hb, Hct, MCV,

Table 1. Laboratory parameters at 0 and 6 months in patients receiving secukinumab.

	Baseline	At 6th month	p
Hb (g/dL)	12.9±1.8	13.2±1.8	>0.05
Htc (%)	40.2±4.9	41.1±5.2	>0.05
MCV (fL)	83.2±6.7	83.9±7.7	>0.05
MCHC (g/dL)	32.06±2.24	32.14±1.26	>0.05
RDW (%)	14.9±1.7	14.7±2.0	>0.05
WBC (µL)	7353.6±2272.6	6981.7±2914.3	>0.05
Neutrophil (%)	60.3±9.6	59.6±8.8	>0.05
Lymphocyte (%)	28.7±8.6	29.3±7.5	>0.05
Platelet (µL)	304,389±102,670	283,028±63,264	>0.05
MPV (fL)	8.2±0.9	8.2±1.1	>0.05
Eosinophil (%)	2.3±1.9	2.1±1.3	>0.05
Glucose (mg/dL)	93.0±19.0	92.8±13.3	>0.05
AST (U/L)	22.1±8.2	24.2±8.4	>0.05
ALT (U/L)	20.8±10.2	23.6±24.8	>0.05
Urea (mg/dL)	34.3±13.0	32.3±1.0	>0.05
Creatinine (mg/dL)	0.9±0.2	0.8±0.4	>0.05
CRP (mg/dL)	16.09±21.7	15.42±34.69	>0.05
ESR (mm/h)	24.8±19.1	20.9±15.3	>0.05

AST: aspartate aminotransferase; ALT: alanine aminotransferase; CBC: complete blood count; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; Hb: hemoglobin; Hct: hematocrit; MCV: mean copuscular volume; MHCH: mean corpuscular hemoglobin concentration; MPV: mean platelet volume; RDW: red cell distribution width; WBC: white blood cell.

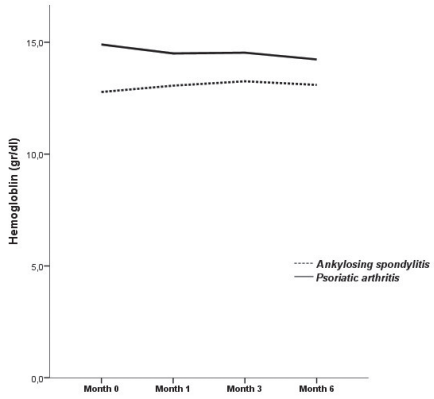

Figure 1. The change in mean hemoglobin levels of study groups.

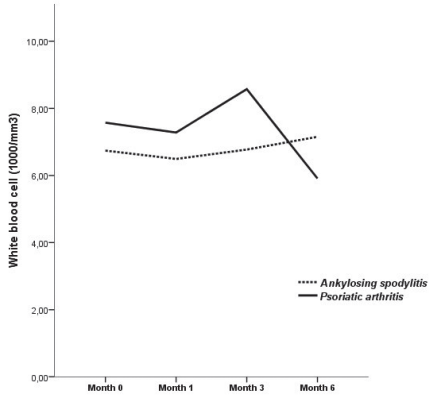

Figure 2. The change in mean white blood cell counts of study groups.

MCHC, lymphocytes, and MPV values of the patients were 13.2±1.8 g/dL; 41.1±5.2%; 83.9±7.7 fl; 32.14±1.26 g/dL; 29.3±7.5%; and 2.8±1.1, respectively, at the 6th month, and these values were slightly higher than the baseline values. However, these differences were not statistically significant (p>0.05). RDW, WBC, neutrophil, platelet, eosinophil, CRP, and ESR values were 14.7±2.0%; 6981.7±2914.3 103/µL; 59.6±8.8%; 283.028±63.264 103/µL; 2.1±1.3%; 15:42±34.69; 20.9±15.3, respectively, at the 6th month, and these values were slightly lower than the baseline values. However, these differences were also not statistically significant (p>0.05) (Figures 1-4). Moreover, there was no statistically significant difference between 0 and 6 months, in terms of liver and kidney function tests.

Differences in hematological data during secukinumab treatment in both males and females were not statistically significant. When analyzed separately for patients with AS and PsA, no negative changes in hematological parameters were observed. In patients responding to secukinumab therapy (ongoing patients), only the Hb level increased significantly (p<0.05), but changes in other study parameters were not statistically significant. In patients

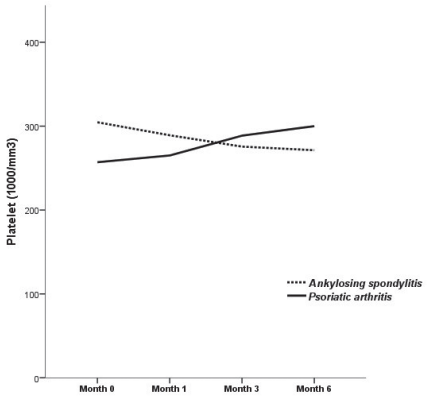

Figure 3. The change in platelet counts of study groups.

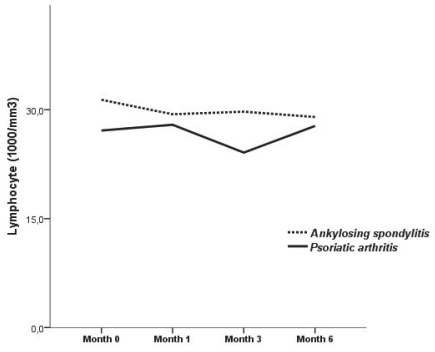

Figure 4. The change in mean lymphocyte counts of study groups.

who did not continue secukinumab treatment due to ineffectiveness and/or adverse events, there were no statistically significant changes in hematological data as long as they continued the treatment.

Discussion

Secukinumab is used in the treatment of AS, PsA, and psoriasis. The most common problem in the side effect profile of secukinumab is susceptibility to infections. There are case reports, especially developing neutropenia related to hematological side effects (15). In many diseases, such as systemic lupus erythematosus, rheumatoid arthritis, cardiovascular diseases, major depression, and achalasia, the relationship between hematological markers and diseases, and their treatment has been investigated (16-20). These studies have shown that hematological markers can be associated with a wide spectrum of diseases. In our study, we aimed to investigate a subject that has not been studied before. We examined the possible changes in hematological markers during 6th month of secukinumab treatment, a biological agent used in the treatment of patients with AS and PsA.

In the studies, the susceptibility of patients receiving secukinumab therapy to neutropenia has investigated (21, 22); grade 3 neutropenia has been detected in 0.6% (n=33) of patients with psoriasis receiving secukinumab (neutrophil<1000) and grade 4 (neutrophil<500) neutropenia in 0.04% (n=2) of patients. Grade 3 neutropenia has been observed in 0.9% (n=12) and 0.2% (n=3) of patients with PsA receiving secukinumab. Grade 3 neutropenia has been detected in 1.1% (n = 9) of patients with AS receiving secukinumab and grade 4 neutropenia in 0.6% (n=5) of patients (23). In our study, neutropenia was not observed in any of our patients during 6 months of secukinumab treatment. Moreover, no statistically significant differences were observed in WBC, neutrophil, platelet, and eosinophil values.

In patients receiving secukinumab, CRP and ESR levels have been statistically shown to decrease significantly compared with the placebo arm (21). In another study evaluating the secukinumab treatment response, treatment has shown to be effective in both patients with normal and high baseline CRP levels. In addition, it has been shown that the treatment response is higher in patients with high baseline CRP levels (24). In our study, a slight decrease in CRP and ESR levels was detected after 6 months of secukinumab treatment. However, the simultaneous, parallel decline in hematological markers and CRP and ESR may suggest that hematological markers may also be used in the evaluation of treatment response. However, because 23 of our patients were also using NSAID, the observed changes could not be related to only secukinumab. The fact that patients could be taking both steroid and non-steroid drugs should not be ignored in other studies on this subject (25).

Considering the data of our study, there was an increase in the Hb and Hct values at the 6th month of the treatment although it was not statistically significant. As with all chronic diseases, chronic disease anemia is common in rheumatological diseases (26). When the results of our patients were examined, it was interpreted that chronic disease anemia could be prevented as a result of suppression of inflammation with treatment, thus increasing the Hb and Hct values.

It is known that some drugs, such as methotrexate and leflunomide, can show hepatotoxic effects (27). The drug prospectus of secukinumab also contains a warning that it may rarely increase liver enzymes. However, it should be noted that hepatosteatosis, which develops on the ground of some diseases such as psoriasis, can also elevate the levels of liver enzymes (28). In our study, AST and ALT values

remained within normal ranges for 6 months in patients receiving secukinumab.

Our study has some limitations. The main limitations of our study are that the hematological markers were not evaluated together with the disease activity scores, our study was a cross-sectional study, the number of patients was small, and the enrolled patient population composed of only young patients.

As a result, drugs used in rheumatology practice may have some undesirable effects on hematological parameters. In our study, no negative effects on hematological parameters were observed in patients with AS and PsA who received secukinumab therapy.

Ethics Committee Approval: Ethics committee approval was received for this study from the Non-Interventional Research Ethics Committee of Fırat University (Approval Date: May 29, 2020; Approval Number: 2020/08-01).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

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Conflict of Interest: The authors have no conflict of interest to declare.

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