Dermatology Practical & Conceptual

Can Biologic Agents Improve Treatment Success in Obese Patients With Psoriasis Vulgaris: A Retrospective Review of 320 Patients With Psoriasis Vulgaris

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ABSTRACT

Introduction: Obesity plays a major role in the development of many inflammatory disorders including psoriasis.

Objectives: We aimed to demonstrate how treatment responses change according to body mass index (BMI) among patients with psoriasis.

Methods: In our study, Psoriasis Area and Severity Index (PASI) 75 and PASI 90 responses were assessed at baseline and at months 1 and 3 among patients who received TNF-α inhibitors, ustekinumab, IL-17 blockers, and IL-23 blockers. The same responses were also assessed with methotrexate and acitretin for a comparison group. Analyses were performed retrospectively.

Results: The study included 317 patients who received 222 biological and 95 conventional treatments. In the group with BMI ≥30, the proportion of patients who achieved PASI 75 response was 40.0% (N = 26) at month 1 and 55.4% (N = 36) at month 3. The proportion of patients who achieved PASI 90 response was 33.8% (N = 22) at month 1 and 44.6% (N = 29) at month 3 among those receiving biological agents. Improvement was significantly more difficult among obese patients. The proportion of patients who achieved PASI 75 response was 3.6% at month 1 and 25.0% (N = 7) at month 3

among patients receiving conventional systemic treatments. While the presence of joint involvement affected the success of treatment among obese patients with psoriasis, no relationships were found for smoking, the presence of concomitant psychiatric diseases, or the presence of pruritus in psoriasis.

Conclusions: Biological agents were more successful in achieving PASI 75 and PASI 90 responses in both non-obese and obese individuals. Based on our study, among biological agents, IL-17 and IL-23 inhibitors may be more successful among obese individuals, but neither of them shows superiority over the other.

Introduction

Psoriasis is a chronic, immune-related, systemic inflammatory disease that may be accompanied by many comorbid conditions including psoriatic arthritis, cardiovascular disorders, cancer, depression, metabolic syndrome, and obesity [1-5].

Morphologically, the skin has an erythematous and scaly appearance in cases of psoriasis; this is due to overstimulation of keratinocytes as well as increased angiogenesis of dilated blood vessels and infiltration of T lymphocyte-associated immune cells [6,7].

Obesity plays a major role in the development of many disorders by increasing insulin resistance and fatty acid synthesis. It also increases fatty acid release from visceral adipose tissues to organs such as the liver and skeletal muscles [8,9]. If nutritional choices remain similar to the current preferences, it is estimated that 38% of the world population will be overweight with body mass index (BMI) values >25 and 20% will be obese with BMI >30 in 2030 [8]. Obesity is involved in the etiopathogenesis of many skin disorders including acanthosis nigricans, acne, hyperhidrosis, intertriginous dermatitis, and acrochordons [10]. In addition, obesity may be accompanied by plantar hyperkeratosis, cellulitis, keratosis pilaris, stria distensae, hidradenitis suppurativa, and skin infections [11-13]. Obesity is also an independent risk factor for psoriasis. The increase in the incidence and prevalence of obesity is almost parallel to clinical exacerbation in the course of psoriasis [14].

Objectives

In this study, patients with BMI values ≥30 were defined as obese while those with BMI <30 were defined as non-obese. We collected data regarding improvement in the Psoriasis Area and Severity Index (PASI) 75 and PASI 90 scores of patients with psoriasis receiving biological agents and conventional treatments. We retrospectively assessed the data and compared the findings according to the patients BMI values. In addition, we assessed biological agents and conventional agents (methotrexate and acitretin) in terms of success in achieving PASI 75 and PASI 90 responses based on the presence of joint involvement, smoking habit, concomitant presence of psychiatric disease, and pruritus.

Methods

This study was conducted in the Chronic Diseases Unit of the Dermatology Department of the Health Sciences University Kayseri Teaching and Research Hospital. Since 2016, all patients were registered with the PSORTAXIS database [15]. The database was updated periodically with data from follow-up, and photographs at baseline and after treatment were also added to the PSORTAXIS database. Treatments were changed based on treatment responses during follow-up. Most of the patients are still attending regular follow-up appointments. In the course of the present study, the electronic database was screened for patients with plaque psoriasis and the records of these patients were extracted. Patients receiving biological agents and conventional agents were included in the research as the study and control groups, respectively.

Inclusion Criteria

Patients aged ≤18 years diagnosed with psoriasis vulgaris who received any systemic agents (biological agents, methotrexate, or acitretin) for therapeutic purposes.

Exclusion Criteria

Psoriasis patients with a diagnosis other than psoriasis vulgaris (nail psoriasis, pustular psoriasis, erythrodermic psoriasis, etc); patients aged <18 years; those receiving topical treatment alone; those with small intestine disorders (celiac disease, enteropathy, etc), pancreas disorders, or hepatobiliary disorders that may affect drug levels or BMI; those with diseases that may cause lymphatic obstruction (tuberculosis, lymphoma, etc.); those with any malignancies; and those with renal or hepatic failure.

In this study, TNF-α inhibitors (adalimumab, etanercept, infliximab, and certolizumab pegol), an IL12/13 inhibitor (ustekinumab), IL-17 blockers (secukinumab and

ixekizumab), and IL-23 blockers (risankizumab and guselkumab) were assessed as biological agents. In addition, methotrexate and acitretin were assessed as systemic conventional agents.

BMI was calculated for all patients using the following formula: BMI = weight (kg)/height^2 (m^2). The patients were classified as obese (BMI ≥30 mg/m^2) and non-obese (BMI <30 mg/m^2; normal and overweight). PASI 75 and PASI 90 responses were assessed at baseline and at months 1 and 3, and percentage changes were recorded for the PASI scores. The achievement of PASI 75 or PASI 90 response was considered as the criterion of success for each individual agent used.

Approval for this study was obtained from the Ethics Committee of Kayseri City Education and Research Hospital (21.02.2023/800).

Statistical Analysis

The normal distribution of the data was tested using the Shapiro-Wilk test and histograms. Data with normal distribution are presented as mean ± standard deviation while data with skewed distribution are presented as median (min-max). Categorical data were analyzed using the chi-square test and Fisher exact test. Continuous data with normal distribution were analyzed using Student t-test while nonparametric data with skewed distribution were analyzed using the Mann-Whitney U test. All data analyses were performed using IBM SPSS Statistics 23.0 (IBM Corp.).

Results

This study included 317 patients who received 222 biological and 95 conventional treatments. The mean age was 45.2 years in the entire study population, while it was 47.6±12.1 years among patients treated with biological agents and 46.1±12.2 years among patients treated with conventional agents, with no significant difference between these groups (P = 0.075) (Table 1). In the group treated with biological agents, the highest mean age was found for ixekizumab while the lowest mean age was found for guselkumab (Table 2).

There were 127 men (57%) and 95 women (43%) in the group treated with biological agents while there were 63 men and 32 women in the group treated with conventional agents, indicating no significant difference in genders between the groups (P = 0.310).

The mean BMI was 28.2±5.3 kg/m^2 in the group treated with biological agents and 27.6±5.9 kg/m^2 in the group treated with conventional agents. The groups were comparable regarding BMI (P = 0.360). Furthermore, there was no significant difference in BMI between patients treated with different conventional agents (P = 0.264).

Among these patients with psoriasis vulgaris, the mean disease duration was 17.7±10.5 years for patients treated with biological agents while it was 10.1±7.9 years for patients treated with conventional agents, and the difference was significant (P < 0.001). The mean disease duration was 15.4±10.4 years for the entire study population.

Of the patients treated with biological agents, 65.3% (N = 145) were biological-naive patients at baseline while 34.7% (N = 77) had switched from a different biological agent. The most commonly used biological agent after switching was secukinumab (52.5%; N = 31) (Table 3).

Patients with BMI <30

Among the patients who had achieved PASI 75 at month 1, the highest rate was observed with ixekizumab (81.8%; N = 9) while the lowest rate was observed with etanercept (12.5%; N = 1) (Table 4).

The proportion of patients who achieved PASI 75 response was 13.4% at month 1 and 29.90% (N = 20) at month 3 among patients treated with conventional agents (Table 5).

Among those treated with biological agents, the proportion of patients who achieved PASI 75 response was 49.0% (N = 77) at month 1 and 70.1% (N = 110) at month 3, while

Table 1. Characteristics of patients receiving biologic agents and conventional systemic therapy.

Continuous Variables	Biologics (All) (N = 222)	Conventional treatment (N = 103)	MTX (N = 57)	Acitretin (N = 46)
Age (years)/mean±SD	46.14±12.16	42.99±13.88	41.65±13.34	44.65±14.51
Body mass index mean±SD	28.15±5.31	27.09±6.05	27.35±6.04	26.75±6.12
PASI improvement during the first month	66.67(-150-100)	40.00(0-100)	33.33(0-100)	50.00(0-100)
PASI improvement during the third month	100±(-150-100)	50.00(0-100)	50.00(0-100)	50.00(0-100)
Duration of the disease (years), mean ±SD	17.68±10.54	9.74±7.77	10.42±7.29	8.89±8.33

MTX = methotrexate; PASI = Psoriasis Area and Severity Index; SD = standard deviation.

Table 2. Age, body mass index, duration of disease and Psoriasis Area and Severity Index improvements in patients receiving biologic agents.

Continuous Variables	ADALIMUMAB (N = 39)	ETANERCEPT (N = 10)	INFLIXIMAB (N = 14)	SERTOLIZUMAB PEGOL (N = 10)	USTEKINUMAB (N = 56)	SECUKINUMAB (N = 59)	IXEKIZUMAB (N= 16)	RISANKIZUMAB (N = 10)	GUSELKUMAB (N = 8)
Age (years) mean ±SD	49.69±12.49	45.90±11.86	48.07±10.35	43.00±16.50	47.91±10.83	47.47±10.30	49.00±9.64	46.50±6.98	41.63±8.78
Body mass index mean ±SD	27.46±4.89	27.19±3.19	28.07±6.27	29.84±6.14	28.74±6.24	27.64±4.34	30.03±6.46	27.41±4.90	26.26±3.94
PASI improvement during the first month	75.00 (-100-100)	50.00(0-75)	55.00 (-150-100)	61.90 (25-100)	66.67 (-50-100)	71.43 (0-100)	83.97 (33-100)	30.95 (0-100)	50 (25-100)
PASI improvement during the third month	100 (-100-100)	66.67 (0-100)	56.25 (-150-100)	72.50 (25-100)	100 (-100-100)	100 (-100-100)	100 (33-100)	60.71 (0-100)	70.83 (50-100)
Duration of the disease (years) mean ±SD	20.85±13.94	18.40±8.89	16.21±8.88	17.00±10.72	16.88±10.13	18.97±10.32	14.81±6.94	12.60±6.62	13.00±6.67

PASI = Psoriasis Area and Severity Index; SD = standard deviation.

Table 3. The percentages of patients are shown according to obesity, smoking, psychiatric disease, joint involvement and pruritus (percentages related to the switching of drugs are also shown in the table).

	OBESITY	SWITCH	SMOKING	PHSYCHIATRIC DISEASE	JOINT INVOLVEMENT	PRURITIS
TOTAL (BIOLOGIC)	28.6% (N=65)	23.7% (N=77)	53.6% (N=119)	16.7% (N=37)	31.9% (N=71)	77.0% (N=171)
ADALIMUMAB	25.6% (N=10)	17.9% (N=7)	53.8% (N=21)	15.4% (N=6)	34.2% (N=13)	74.4% (N=29)
ETANERCEPT	20.0% (N=2)	20.0% (N=2)	50.0% (N=5)	0.0% (N=0)	44.4% (N=4)	70.0% (N=7)
INFLIXIMAB	28.6% (N=4)	21.4% (N=3)	57.1% (N=8)	21.4% (N=3)	42.9% (N=6)	92.9% (N=13)
SERTOLIZUMAB	40.0% (N=4)	40.0% (N=4)	40.0% (N=4)	10.0% (N=1)	57.1% (N=4)	70.0% (N=7)
USTEKINUMAB	30.4% (N=17)	17.9% (N=10)	64.3% (N=36)	14.3% (N=8)	26.5% (N=13)	73.2% (N=41)
SECUKINUMAB	32.2% (N=19)	52.5% (N=31)	47.5% (N=28)	23.7% (N=14)	38.0% (N=19)	78.0% (N=46)
IXEKIZUMAB	31.3% (N=5)	50.0% (N=8)	50.0% (N=8)	6.3% (N=1)	28.6% (N=4)	81.3% (N=13)
RISANKIZUMAB	20.0% (N=2)	60.0% (N=4)	40.0% (N=4)	10.0% (N=1)	40.0% (N=4)	90.0% (N=9)
GUSELKUMAB	25.0% (N=2)	75.0% (N=6)	62.5% (N=5)	37.5% (N=3)	57.1% (N=4)	75.0% (N=6)
TOTAL (CONVENTIONAL)	27.2% (N=28)	----------	54.4% (N=)	22.3% (N=23)	17.4% (N=18)	81.5% (N=103)
METHOTREXATE	31.6% (N=18)	----------	54.4% (N=31)	21.1% (N=12)	17.5% (N=10)	82.5% (N=47)
ACITRETIN	21.7% (N=10)	----------	58.7% (N=27)	23.9% (N=11)	17.4% (N=8)	80.4% (N=37)

the proportion of patients who achieved PASI 90 response was 33.8% (N = 53) at month 1 and 58.6% (N = 92) at month 3 (Table 5).

In the group treated with conventional systemic agents, the proportion of patients who achieved PASI 90 response was 9.0% (N = 6) at month 1, and this figure increased to 23.9% (N = 16) at month 3.

Patients with BMI ≥30

The proportion of patients who achieved PASI 75 response was 40.0% (N = 26) at month 1 and 55.4% (N = 36) at month 3 among patients treated with biological agents. The highest rate was observed with ixekizumab (60.0%; N = 3) while the lowest rate was observed with etanercept (0%; N = 0).

The proportion of patients who achieved PASI 75 response was 3.6% at month 1 and 25.0% (N = 7) at month 3 among patients treated with conventional agents.

The proportion of patients who achieved PASI 90 response was 33.8% (N = 22) at month 1 and 44.6% (N = 29) at month 3 among patients treated with biological agents (Table 5). The highest rate was observed with ixekizumab (42.1%; N = 8) (Table 6). In the group treated with conventional systemic agents, no patient achieved PASI 90 response at month 1, while the proportion of patients who achieved PASI 90 response at month 3 was 3.6% (N = 1) (Table 5).

In summary, when the entire study population was considered, BMI was ≥30 kg/m^2 for 224 patients and <30 kg/m^2 for 93 patients. The PASI assessments changed as seen in Table 7 when the entire study population was not classified into treatment groups. At month 3, PASI scores showed improvement in 48.2% (N = 108) of the non-obese patients and 32.3% (N = 30) of the obese patients. The rate of improvement was significantly worse among obese patients (P = 0.009). Although a difference could be observed at month 1, it was not reflected at the same extent in our entire study population (P = 0.063). For PASI 75 response, there was improvement in favor of non-obese patients at months 1 and 3, but these differences did not reach statistical significance (P = 0.124 and P = 0.673, respectively).

Table 4. PASI 75 and PASI 90 responses during the first and third months in patients with a body mass index <30 (normal and overweight) when the biologics were evaluated separately.

Continuous Variables	ADALIMUMAB (N=29)	ETANERCEPT (N=8)	INFLIXIMAB (N=10)	SERTOLIZUMAB PEGOL (N=6)	USTEKINUMAB (N=39)	SECUKINUMAB (N=39)	IXEKIZUMAB (N=12)	RISANKIZUMAB (N=8)	GUSELKUMAB (N=6)	Total biologic (N=157)
Patients who achieved PASI 75 during the first month	48.3% (N=14)	12.5% (N=1)	50% (N=5)	33.3% (N=2)	53.8% (N=21)	52.5% (N=21)	81.8% (N=9)	25% (N=2)	33.3% (N=2)	49.0% (N=77)
Patients who achieved PASI 75 the third month	69.0% (N=20)	37.7% (N=3)	40.0% (N=4)	50.0% (N=3)	76.9% (N=30)	84.5% (N=33)	100% (N=11)	50.0% (N=4)	33.3% (N=2)	70.1% (N=110)
Patients who achieved PASI 90 the first month	31.0% (N=9)	0.0% (N=0)	50.0% (N=5)	0.0% (N=0)	48.7% (N=19)	33.3% (N=13)	45.5% (N=5)	12.5% (N=1)	16.7% (N=1)	33.8% (N=53)
Patients who achieved PASI 75 the third month	58.6% (N=17)	12.5% (N=1)	30.0% (N=3)	33.3% (N=2)	69.2% (N=27)	67.5% (N=27)	100% (N=11)	37.5% (N=3)	16.7% (N=1)	58.6% (N=92)

PASI = Psoriasis Area and Severity Index.

Table 5. Patients were classified into two groups as those treated with biological agents and conventional agents. No significant difference was observed in the achieving of PASI 75 and PASI 90 responses during the first and third months

	BIOLOGICAL			CONVENTIONAL		
	BMI <30 (N=157)	BMI >30 (N=65)	P	BMI <30 (N=67)	BMI >30 (N=28)	P
PASI 75 during the first month	49.0% (N=77)	40.0% (N=26)	0.239	13.4% (N=9)	3.6% (N=1)	0.272
PASI 90 during the first month	33.8% (N=53)	33.8% (N=22)	1.000	9.0% (N=6)	0.0% (N=0)	0.175
PASI 75 during the third month	70.1% (N=110)	55.4% (N=36)	0.044	29.9% (N=20)	25.0% (N=7)	0.804
PASI 90 during the third month	58.6% (N=92)	44.6% (N=29)	0.075	23.9% (N=16)	3.6% (N=1)	0.014

BMI = body mass index; PASI = Psoriasis Area and Severity Index.

When patients were classified into two groups as those treated with biological agents and conventional agents, no significant difference was observed in achieving PASI 75 and PASI 90 responses at months 1 and 3 (Table 5). At month 3, the proportion of patients who achieved PASI 75 response was 70.1% (N = 110) among non-obese patients and 44.6% (N=29) among obese patients treated with biological agents, reflecting a significant difference (p=0.044). A similar trend was observed for PASI 90 achievement at month 3 in favor of non-obese patients (p=0.075). Among patients treated with conventional agents, the difference was statistically significant (P = 0.014).

Joint Involvement

It is apparent that joint involvement is a good predictor for achievement of PASI 75 and PASI 90 responses (P = 0.007 for PASI 75 at month 1, P = 0.044 for PASI 90 at month 1; P = 0.003 for PASI 75 at month 3; P = 0.011 for PASI 90 at month 3).

Joint involvement was more common among older patients. The mean age was 49.2±10.2 years among patients with joint involvement and it was 45.6±11.9 years among those without joint involvement (P = 0.013).

Disease duration showed no significant difference regarding joint involvement. The mean disease duration was 15.8±9.4 years among patients with joint involvement and 14.5±10.8 years among those without joint involvement (P = 0.366).

Pruritus

There was no significant correlation between pruritus and achievement of PASI 75 and PASI 90 responses at months 1 and 3 (P = 0.338 for PASI 75 at month 1, P = 0.502 for PASI 90 at month 1; P = 0.64 for PASI 75 at month 3, P =0.110 for PASI 90 at month 3). At month 3, the rates of achieving PASI 75 and PASI 90 responses were better among patients without pruritus.

Psychiatric Disorders

There was a concomitant psychiatric disorder among 16.7% (N = 37) of the patients treated with biological agents and 22.3% (N = 23) of the patients treated with conventional agents (P = 0.121).

Smoking

There was no significant correlation between smoking and the achievement of PASI 75 and PASI 90 responses at months 1 or 3 (P = 0.420 for PASI 75 at month 1, P = 0.322 for PASI 90 at month 1; P = 0.670 for PASI 75 at month 3, P =0 .591 for PASI 90 at month 3).

Conclusions

Psoriasis develops when an interaction occurs between keratinocytes and immune cells. It may be induced by damage to the keratinocytes due to congenital immune system activation or neutrophil activation due to infection, increased angiogenesis, and dendritic cell activation [16]. The IL-23 released from dendritic cells converts T cells into Th-17 cells to produce IL-17 and IL-22. As a result, psoriatic plaque formation starts due to keratinocyte hyperproliferation and differentiation. In brief, the IL-23/Th17 axis plays a pivotal role in the pathogenesis of psoriasis [16-18].

Obesity is considered an independent risk factor for psoriasis, increasing the risk of psoriasis development. It has been reported that each 1 kg/m^2 increase in BMI corresponds

Table 6. PASI 75 and PASI 90 responses during the first and third months in patients with a BMI >30 (obese) when the biologics were evaluated separately.

Continuous variables	ADALIMUMAB (N=10)	ETANERCEPT (N=2)	INFLIXIMAB (N=4)	SERTOLIZUMAB PEGOL (N=4)	USTEKINUMAB (N=17)	SECUKINUMAB (N=19)	IXEKIZUMAB (N=5)	RISANKIZUMAB (N=2)	GUSELKUMAB (N=2)	Total biologic (N=65)
Patients who achieved PASI 75 the first month	60.0% (N=6)	0.0% (N=0)	25.0% (N=1)	50.0% (N=2)	35.3% (N=6)	42.1% (N=8)	60.0% (N=3)	0.0% (N=0)	0.0% (N=0)	40.0% (N=26)
Patients who achieved PASI 75 the third month	80.0% (N=8)	100% (N=2)	25.0% (N=1)	50.0% (N=2)	47.1% (N=8)	52.6% (N=10)	60.0% (N=3)	0.0% (N=0)	100.0% (N=2)	55.4% (N=36)
Patients who achieved PASI 90 the first month	60.0% (N=6)	0.0% (N=0)	25.0% (N=1)	25.0% (N=1)	23.5% (N=4)	42.1% (N=8)	40.0% (N=2)	0.0% (N=0)	0.0% (N=0)	33.8% (N=22)
Patients who achieved PASI 75 the third month	70.0% (N=7)	0.0% (N=0)	25.0% (N=1)	50.0% (N=2)	35.3% (N=6)	47.4% (N=9)	60.0% (N=3)	0.0% (N=0)	50.0% (N=1)	44.6% (N=29)

PASI = Psoriasis Area and Severity Index.

Table 7. The PASI assessments changed as shown below when the entire study population was not classified into treatment groups during the first and third months.

	BMI <30 (N=224)	BMI >30 (N=93)	P
PASI 75 the first month	38.4% (N=86)	29.0% (N=27)	0.124
PASI 90 the first month	58.0% (N=130)	46.2% (N=43)	0.063
PASI 75 the third month	26.3% (N=59)	23.7% (N=22)	0.673
PASI 90 the third month	48.2% (N=108)	32.3% (N=30)	0.009

BMI = body mass index; PASI = Psoriasis Area and Severity Index.

to an approximately 4% increase in the risk of psoriasis development [19,20]. In systematic reviews, it was emphasized that excessively high BMI values are positively associated with disease severity in cases of psoriasis [18,21].

Unlike other adipokines, the adiponectin level decreases in the presence of obesity. A similar decrease is also seen in patients with psoriasis [22-24].

At months 1 and 3, patients treated with biological agents (N = 222) had superior results compared to patients treated with conventional agents (N = 95; methotrexate and acitretin) in terms of achieving PASI 75 and PASI 90 responses in both groups of patients with BMI ≥30 kg/m^2 and <30 kg/m^2 in the present study. This adversely affected treatment success in the group with BMI ≥30 kg/m^2. Similarly, previous studies found that high BMI values increase disease activity and make it difficult to respond to biological treatment agents [1, 3].

IL-17 inhibitors (ixekizumab and secukinumab) and IL-23 inhibitors (risankizumab and guselkumab) may be better alternatives for obese individuals compared to other biological and systemic conventional treatments (methotrexate and acitretin). These agents have higher treatment success and fewer adverse effects compared to systemic conventional treatments; they can facilitate the achievement of PASI 75 and PASI 90 responses more readily. In a study by Anghel et al., it was observed that obese patients responded more poorly to TNF-α inhibitors and IL-12/23 inhibitors compared to IL-17 and IL-23 inhibitors [6]. In our study, we assessed risankizumab and guselkumab, which were recently introduced in the treatment of psoriasis. These agents may be better therapeutic alternatives for obese patients.

In our study, ixekizumab achieved the best and fastest rates of PASI 75 response at months 1 and 3 compared to other biological agents. The PASI 75 response rate was 75% (N = 12/16) at month 1 and 87.5% (N = 14/16) at month 3. Etanercept (10%; N = 1/10) and infliximab (35.7%; N = 5/14) seemed to be the weakest agents regarding achievement of PASI 75 response at months 1 and 3.

Regarding PASI 90 response, there was no significant difference among biological agents at month 1. However, ixekizumab seemed more successful at month 3 (87.5%; N = 14/16). Only one patient achieved PASI 90 response at month 3 with etanercept.

When the rates of PASI 90 response were considered, no significant difference was observed among biological agents at moth 1, while ixekizumab seemed better at month 3 (87.5% (N = 14/16). At month 3, etanercept seemed to be the weakest agent regarding PASI 90 response as only one patient in this subgroup achieved PASI 90.

A recent meta-analysis supports the findings of the present study [26]. According to that meta-analysis, infliximab, ixekizumab, brodalumab, secukinumab, risankizumab, and guselkumab were superior to ustekinumab and three other TNF-α inhibitors (adalimumab, certolizumab, and etanercept) in terms of PASI 90 response rates. Ustekinumab and adalimumab were also superior to etanercept. These findings are in agreement with our study. In another meta-analysis, it was suggested that IL-17, IL-12/23, and IL-23 inhibitors have comparable efficacy profiles in terms of PASI 75 and PASI 100 response rates and that these agents are superior to TNF-α inhibitors [27].

Guselkumab was the most commonly used agent after switching treatments (75%; N = 6); however, the number of patients who received secukinumab after switching was highest (N = 31) (Table 3). Adalimumab and etanercept (TNF-α inhibitors) were the most commonly changed biological agents.

In our study, it was seen that smoking habit was not a significant parameter in terms of achieving PASI 75 or PASI 90 responses in the groups of patients with BMI of <30 and BMI of ≥30 in comparisons among biological agents or when biological agents were compared with systemic conventional agents. Based on a meta-analysis, it is known that smoking facilitates drug-induced psoriasis development in patients with inflammatory bowel disease, and it was also reported that obesity further increases the risk of drug-induced psoriasis [28,29].

The rate of concomitant psychiatric disorders was higher in the group treated with biological agents (16.7%; N = 37) compared to the group treated with systemic conventional agents (22.3%; N = 23) (P = 0.121). Based on this finding, it can be suggested that higher rates of treatment success and better profiles of adverse effects with the use of biological agents compared to systemic conventional agents may have improved the psychological status of the patients. In a study of 91 patients in which the risk of psychiatric illness and suicide was investigated, it was reported that the risk of

psychiatric illness and suicide increased with the incidence of comorbidities, and therefore all patients with psoriasis should be receive psychiatric evaluation [30]

According to a meta-analysis, joint involvement in cases of psoriasis mostly develops among patients with more common and severe skin lesions and higher PASI scores [31]. It was also suggested that joint involvement is not related to disease type (plaque, guttate, pustular, erythrodermic, etc) [32]. It is important to diagnose joint involvement in psoriasis as permanent joint damage may occur at as early as 6 months among untreated cases [33,34]. It is currently unclear which patients with psoriasis will develop joint involvement; however, there are some factors implied in joint involvement. Obesity, trauma, nail dystrophy, and the localization of psoriasis lesions (scalp and intergluteal region) may be predictive of potential joint involvement [32,34]. In our study, the joint involvement rate was lower in the group treated with biological agents (35.9%; N = 71) compared to patients treated with systemic conventional agents (17.4%; N = 18), and this difference was significant (P = 0.003). This may be due to the longer disease duration and cases being more refractory to other treatments among the patients treated with biological agents. It is apparent that joint involvement is a good predictor of the achievement of PASI 75 and PASI 90 responses.

Pruritus was more common among patients treated with systemic conventional agents (86.5%; N = 45) compared to those treated with biological agents (77%; N = 171). Pruritus seemed to be slightly more common in cases of chronic and refractory disease.

When all patients treated with biological agents and systemic conventional agents were compared, it was found that biological agents were more successful in achieving PASI 75 and PASI 90 responses among both obese and non-obese patients. Non-obese patients achieved PASI 75 and PASI 90 responses more readily than obese patients. Based on our results, new generation biological agents (secukinumab, ixekizumab, risankizumab, and guselkumab) may be used by obese patients without any superiority of one drug over the others. Given that these agents have more favorable adverse effect profiles than systemic conventional agents, it would be more appropriate to prescribe these agents rather than TNF-α inhibitors or ustekinumab (IL12/23 inhibitor). For patients with joint involvement, treatment with biological agents may be considered in the early stages of the disease.

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