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Effects of biologic drug therapy on body weight, appetite, and blood lipid profile in patients with psoriasis

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Abstract

Obesity and dyslipidemia are frequently observed in patients with psoriasis. This study aimed to evaluate the effects of biological therapy on body weight (BW), body mass index (BMI), appetite, and blood lipid profiles in patients with psoriasis. A total of 83 patients receiving biologic therapy (n=44) [anti-tumor necrosis factor alpha (anti-TNFα) (n=5), interleukin (IL)-12/23 inhibitor (n=13), IL-17 inhibitor (n=20), and IL-23 inhibitor (n=6)] and conventional therapy (n=39) [methotrexate (MTX) (n=25) and acitretin (n=14)] were included in the study. The patient's baseline and current BW, BMI, waist circumference, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), plasma triglyceride values, and Psoriasis Area and Severity Index (PASI) were retrospectively screened. Appetite was assessed with the Simplified Nutritional Appetite Questionnaire (SNAQ). The mean BW percent change values were found to increase by 2.40±2.30 kg, 2.38±4.13 kg, and 0.40±3.47 kg in patients taking anti-TNFα, IL-12/23 inhibitor, and IL-17 inhibitor agents, respectively, decrease by -0.60±0.89 kg in those receiving an IL-23 inhibitor; increase by 0.52±3.40 kg and 1.38±2.79 kg in those receiving MTX and acitretin, respectively. The triglyceride percent change rates increased with MTX (27.46±52.87 mg/dl) (p=0.029). Anti-TNFα and ixekizumab increased HDL percent change rates (21.44±20.99 mg/dl and 24.4±35.40 mg/dl, respectively) (p=0.044 and p=0.005). Although the SNAQ scores were similar in patients using conventional and biological drugs, a negative correlation was observed between the SNAQ scores and the PASI change (p=0.049, r=-0.221). In addition, an increase in BMI had a negative correlation with the PASI change (p=0.01, r=-0.282). Anti-TNFα and IL-12-23 inhibitors increased BW. While MTX increased triglyceride levels, anti-TNFα and ixekizumab increased HDL levels. In the treatment of psoriasis, the presence of obesity and blood lipid profiles should be considered in the selection of the appropriate treatment for each patient.

Keywords: Anti-TNFa, appetite, biologic therapy, body weight, psoriasis, ustekinumab

Introduction

Psoriasis is a chronic, inflammatory disease that affects the skin and joints and has an incidence of approximately 2% in the general population [1]. The disease follows a chronic course characterized by erythematous-squamous plaques on the skin, with remissions and relapses. Increased epidermal cellular turnover secondary to abnormal immunological interactions between keratinocytes and inflammatory cells is responsible for forming psoriatic plaques. The most important cytokines involved in this process are tumor necrosis factor-alpha (TNFα), interleukin (IL)-23, IL-17, and IL-22 [2].

Conventional drugs, such as acitretin and methotrexate (MTX) are the first choice in treating moderate/severe psoriasis. Biologic drugs are used in patients who do not benefit from conventional therapy or in cases where these drugs are contraindicated. Among the biologics used, etanercept, infliximab, adalimumab, and certolizumab have effects on anti-TNFα. At the same time, ustekinumab provides targeted therapy by blocking IL-12/23, secukinumab and ixekizumab by blocking IL-17, and guselkumab and risankizumab by blocking IL-23 [2].

It has been shown that there is an increase in systemic inflammation in psoriasis. Some comorbidities in which the inflammatory process is dominant, such as obesity, dyslipidemia, cardiovascular diseases, insulin resistance, uveitis, and

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inflammatory bowel diseases are more common in patients with psoriasis than in the healthy population [3]. Obesity is observed in 12-35% of patients with chronic plaque psoriasis [4,5]. There is a bidirectional relationship between psoriasis and obesity. While the prevalence of obesity in patients with psoriasis increases over time, psoriasis may also present with a late onset in obese patients without psoriasis. Furthermore, it has been demonstrated that the risk of psoriasis increases by 40% in patients with a body mass index (BMI) of 27-28 kg/m^2; therefore, obesity is recognized as an independent risk factor for the development of psoriasis [6].

Elevated TNFα, IL-1, IL-6, and lipoprotein levels in psoriasis stimulate fat synthesis in the liver, causing dyslipidemia by promoting lipolysis [7]. Patients with psoriasis have a significantly increased risk of hypertension, angina pectoris, and myocardial infarction [8]. Even in patients without additional cardiovascular risk factors, carotid artery intima-media thickness has been shown to increase, and psoriasis is now accepted as an independent risk factor for developing ischemic heart disease [9]. The coexistence of obesity in these patients will further increase the risk of cardiovascular morbidity.

Recent studies have shown increased in body weight (BW) and BMI in patients using anti-TNFα drugs and ustekinumab [10,11]. Some studies have reported that the response to biological therapy is weak in obese patients but treatment resistance can be overcome by reducing BMI [5]. All these findings suggest a complex, multi-faceted interaction between BW and biologics in terms of disease progression and treatment response in patients receiving biologic therapy.

In light of this, we aimed to reveal the effects of biologics on BW, appetite, and plasma lipid profile in patients with psoriasis receiving conventional or biological drug therapy.

Material and Methods

This study was approved by the Non-Invasive Research Ethics Committee of Biruni University (2023/81-30). Between January 2020 and June 2023, patients with psoriasis who were followed up in the dermatology outpatient clinics of Biruni University Hospital and Başakşehir Çam and Sakura City Hospital, aged ≥18 years, and receiving conventional or biological therapy for at least four months were included in the study. Patients with a history of appetite-suppressant or appetite-stimulant drugs, voluntary weight gain or slimming diet, chronic infections in the last three months, and a history of malignancy were excluded from the study.

The patients' sociodemographic data, clinical characteristics, BW (kg), BMI [kg/height (m^2)], waist circumference (cm), total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), plasma triglyceride, fasting blood glucose values, and the Psoriasis Area and Severity Index (PASI) were obtained by retrospectively. The percent changes from the baseline to the last visit were determined. The Simplified Nutritional Appetite Questionnaire (SNAQ) was used to assess the patients' appetite. The PASI score was used to assess psoriasis severity. According to their BMI values, the patients were divided into four obesity groups: <18.5, 18.5-24.9, 25-29.9, and ≥30. The data obtained from the study were compared between the conventional (MTX and acitretin) and biological therapy groups [anti-TNFα (etanercept, adalimumab), IL-12/23 inhibitor (ustekinumab), IL-17 inhibitor (ixekizumab, secukinumab), and IL-23 inhibitor (risankizumab, guselkumab)].

The Statistical Package for the Social Sciences (SPSS, version 25.0. Armonk, NY: IBM Corp.) was used to analyze the data. Mean±standard deviation values were used for numerical variables, numbers and percentages were used for categorical variables. The Student t-test and Mann–Whitney U-test were used to compare independent variables between two groups, while the one-way analysis of variance and Kruskal–Wallis tests were used to compare more than two groups. The Wilcoxon test was conducted for the analysis of dependent variables. Correlation analysis between the data was performed using the Pearson's correlation test. Categorical variables were analyzed with the chi-square and Fisher exact tests. A p-value of <0.05 was considered statistically significant.

Results

The study included 83 patients, of whom 29 (35%) female and 54 (65%) male, with a mean age of 42.6±15.39 years. Thirty-nine patients were receiving conventional treatment [MTX (n=25) and acitretin (n=14)], and 44 patients were receiving biological drug therapy [anti-tumor necrosis factor alpha (anti-TNFα) (etanercept, adalimumab) (n=5), interleukin (IL)-12/23 inhibitor (ustekinumab) (n=13), IL-17 inhibitor (ixekizumab, secukinumab) (n=20), and IL-23 inhibitor (risankizumab, guselkumab) (n=6)].

Sixty (72.2%) of the patients were overweight/obese, and no significant difference was found in the frequency of obesity between the patients using conventional and biologic drugs (p>0.05). There was also no statistically significant difference between the conventional and biological therapy groups in terms of age, gender, comorbidities, disease duration, treatment duration, baseline BW, BMI, waist circumference, total cholesterol, LDL, HDL, triglyceride, or fasting blood glucose values (p<0.05) (Table 1).

Among the patients using biologic drugs, the mean BW percent change values increased by 2.40±2.30, 2.38±4.13, and 0.40±3.47 kg in the anti-TNFα, IL-12/23 inhibitor, and IL-17 inhibitor groups, respectively, decreased by -0.60±0.89 kg in the IL-23 inhibitor group, and increased by 0.52±3.40 and 1.38±2.79 kg in the MTX and acitretin groups, respectively, albeit with no statistically significant difference (p>0.05). The BMI percent change and waist circumference percent change did not statistically significantly differ between the conventional and

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biological therapy groups (p>0.05) (Figure 1). The BMI percent change also did not statistically significantly differ between the obesity groups (p>0.05) (Table 3).

Although the baseline PASI values were similar in both groups, the PASI change statistically significantly differed, being determined to be 76.9±20.20 in the biological drug group and 45.2±82.80 in the conventional drug group (p=0.016) (Table 2). SNAQ scores were similar in patients using conventional and biological drugs, but a negative correlation was observed between the SNAQ scores and the PASI change (p=0.049, r=-0.221) (Tables 2 and 4). In addition, an increase in BMI had a positive correlation with an increase in waist circumference (p=0.000, r=-0.397) and a negative correlation with the PASI change (p=0.01, r=-0.282) (Table 5).

There was a 27.46±52.87 mg/dl increase in the percent change in the triglyceride levels of patients using MTX (p=0.029) (Table 2). HDL percent change rates increased by 21.44±20.99 mg/dl among patients taking anti-TNFα and by 24.4±35.40 mg/dl among those receiving ixekizumab (p=0.044 and p=0.005, respectively) (Figure 2). There was also no relationship between obesity degree and percent changes in blood lipid profile (p>0.05) (Table 3).

Table 1. Clinical and demographic characteristics of patients with psoriasis vulgaris

Clinical and laboratory findings		Treatment group		Total	p
		Conventional	Biologic		
Gender (female/male), n (%)		11/28 (28/72%)	18/26 (41/59%)	29/54 (35/65%)	0.163
Age (years) (mean±SD)		42±17.2	43.2±13.81	42.6±15.39	0.729
Disease duration (month) (mean±SD)		114.5±90.3	173.7±126.6	145.9±114.31	0.018
Treatment duration (month) (mean SD)		12.41±22.06	10.57±12.31	11.43±17.49	0.635
Baseline BW (kg) (mean±SD)		76.9±15.5	81.8±19.2	79.49±17.65	0.213
Baseline BMI (kg/m²) (mean±SD)		27.3±4.9	28.4±6.0	27.86±5.53	0.385
Baseline waist circumference (cm) (mean±SD)		93.6±12.9	94.4±14.00	93.94±13.25	0.804
Baseline triglyceride (mg/dl) (mean±SD)		132.2±64.0	174.8±130.2	154.27±105.31	0.068
Total cholesterol (mg/dl) (mean±SD)		185.0±38.2	168.2±39.2	185.62±38.48	0.884
LDL (mg/dl) (mean±SD)		113.7±33.6	114.7±35.5	114.21±34.39	0.891
HDL (mg/dl) (mean±SD)		46.3±9.4	43.2±12.9	44.68±11.36	0.227
FBG (mg/dl) (mean±SD)		100.7±24.6	106.2±50.5	103.56±39.89	0.541
Overweight/obesity, n (%)	**Present**	26 (67%)	34 (77%)	60 (72.2%)	0.203
	<18.5	3(%8%)	2 (6%)	5 (6%)	
	18.5-24.9	10 (26%)	8 (18%)	23 (27.7%)	
	25-29.9	16 (40%)	18 (40%)	34 (41%)	0.57
	≥30	10 (26%)	16 (36%)	26 (31.3%)	
Smoking, n (%)		13 (33%)	19 (43%)	32 (38.6%)	0.244
Alcohol consumption n (%)		1 (3%)	2 (5%)	3 (3.6%)	0.546
Comorbidities, n (%)	**Present**	9 (23%)	13(30%)	22 (26.5%)	0.552
	Diabetes mellitus	4 (10%)	5 (11%)	9 (10.8%)	0.578
	Cardiovascular disease	1 (3%)	2 (5%)	3 (3.6%)	0.546
	Hypertension	2 (5%)	4 (9%)	6 (7.2%)	0.397
	Dyslipidemia	2 (5%)	2 (5%)	4 (4.8%)	0.645
	Metabolic syndrome	0 (0%)	1 (84%)	1 (1.2%)	0.530
Psoriatic arthritis, n (%)		7 (18%)	7 (16%)	14 (16.9%)	0.517

SD: standard deviation, BW: body weight, BMI: body mass index, LDL: low-density lipoprotein, HDL: high-density lipoprotein, FBG: fasting blood glucose

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Table 2. Comparison of clinical and laboratory data between the treatment subgroups

Clinical and laboratory findings	Treatment group/subgroup		Mean±SD	p
Baseline PASI	**Conventional**	**Methotrexate**	11.24±7.26	0.677
		Acitretin	10.53±9.55	
		Total	11.0±7.90	
	Biologic	**Anti-TNFα**	12.89±7.96	
		IL-17 inhibitor	13.85±6.62	
		Ixekizumab	16.8±7.80	
		Secukinumab	11.4±4.60	
		IL-12/23 inhibitor	14.90±11.24	
		IL-23 inhibitor	11.28±1.94	
		Total	13.8±7.90	
PASI difference (% change)	**Conventional**	**Methotrexate**	-47.74±99.70	***=0.016**
		Acitretin	-39.20±41.94	
		Total*	-45.2±82.80	
	Biologic	**Anti-TNFα**	-75.37±23.55	
		IL-17 inhibitor	-84.06±17.84	
		Ixekizumab	-86.5±19.60	
		Secukinumab	-82.0±16.90	
		IL-12-23 inhibitor	-69.06±21.87	
		IL-23 inhibitor	-68.13±17.23	
		Total*	-76.9±20.20	
BW difference (% change) (kg)	**Conventional**	**Methotrexate**	0.52±3.40	0.353
		Acitretin	1.38±2.79	
		Total	0.77±3.16	
	Biologic	**Anti-TNFα**	2.40±2.30	
		IL-17 inhibitor	0.40±3.47	
		Ixekizumab	-0.1±2.60	
		Secukinumab	0.8±4.10	
		IL-12/23 inhibitor	2.38±4.13	
		IL-23 inhibitor	-0.60±0.89	
		Total	1.09±3.46	
BMI difference (% change)	**Conventional**	**Methotrexate**	1.13±3.92	0.313
		Acitretin	2.12±3.69	
		Total	1.4±3.80	
	Biologic	**Anti-TNFα**	3.74±3.05	
		IL-17 inhibitor	0.65±3.92	
		Ixekizumab	0.0±2.50	
		Secukinumab	1.2±4.80	
		IL-12/23 inhibitor	3.05±5.14	
		IL-23 inhibitor	-0.29±0.48	
		Total	1.6±4.10	
Waist circumference difference (% change)	**Conventional**	**Methotrexate**	0.73±2.88	0.823
		Acitretin	1.72±4.83	
		Total	1.11±3.59	
	Biologic	**Anti-TNFα**	0.88±0.99	
		IL-17 inhibitor	0.28±2.22	
		Ixekizumab	0.64±1.55	
		Secukinumab	-0.4±2.73	
		IL-12/23 inhibitor	1.04±4.02	
		IL-23 inhibitor	-0.28±0.88	
		Total	0.48±2.65	

SD: standard deviation, PASI: Psoriasis Area and Severity Index, BW: body weight, BMI: body mass index, SNAQ: Simplified Nutritional Appetite Questionnaire, LDL: low-density lipoprotein, HDL: high-density lipoprotein, FBG: fasting blood glucose. Different superscripts (*, ‡) indicate statistically significant differences between the mean values in a row ($p<0.05$).

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Table 2. Comparison of clinical and laboratory data between the treatment subgroups

Clinical and laboratory findings	Treatment group/subgroup		Mean±SD	p
SNAQ score	Conventional	Methotrexate	16.21±1.93	0.597
		Acitretin	16.08±1.98	
		Total	16.2±1.90	
	Biologic	Anti-TNFα	16.20±1.10	
		IL-17 inhibitor	16.11±1.53	
		İxekizumab	15.9±1.50	
		Secukinumab	16.3±1.60	
		IL-12/23 inhibitor	15.15±1.95	
		IL-23 inhibitor	15.40±2.07	
		Total	15.7±1.70	
Triglyceride difference (% change)	Conventional	Methotrexate*	27.46±52.87	*=0.029
		Acitretin	-3.28±29.97	
		Total	16.6±47.60	
	Biologic	Anti-TNFα	-16.74±42.65	
		IL-17 inhibitor	-3.84±35.55	
		Ixekizumab	-10.8±37.50	
		Secukinumab	1.9 ±34.60	
		IL-12-23 inhibitor	-6.67±27.37	
		IL-23 inhibitor	19.82±27.23	
		Total	-3.5±33.30	
LDL difference (% change)	Conventional	Methotrexate	-0.28±23.17	0.323
		Acitretin	26.93±72.47	
		Total	7.8±47.20	
	Biologic	Anti-TNFα	4.22±18.66	
		IL-17 inhibitor	3.85±29.77	
		Ixekizumab	11.1±34.90	
		Secukinumab	-2.6±24.30	
		IL-12/23 inhibitor	5.74±17.60	
		IL-23 inhibitor	-9.70±13.50	
		Total	1.9±24.00	
Total cholesterol difference (% change)	Conventional	Methotrexate	1.53±17.00	0.771
		Acitretin	4.66±12.38	
		Total	1.8±16.20	
	Biologic	Anti-TNFα	-4.24±7.82	
		IL-17 inhibitor	-0.59±12.63	
		Ixekizumab	1.6±12.70	
		Secukinumab	-2.6±12.90	
		IL-12/23 inhibitor	3.82±11.09	
		IL-23 inhibitor	-0.86±3.43	
		Total	0.3±10.80	
HDL difference (% change)	Conventional	Methotrexate	0.18±14.85	*=0.044 ‡=0.005
		Acitretin	-4.64±17.59	
		Total	-2.0±16.00	
	Biologic	Anti-TNFα*	21.44±20.99	
		IL-17 inhibitor	10.55±28.80	
		Ixekizumab‡	24.4±35.40	
		Secukinumab	-2.0±13.30	
		IL-12/23 inhibitor	-4.54±11.53	
		IL-23 inhibitor	-3.92±5.70	
		Total	5.9±23.20	

SD: standard deviation, PASI: Psoriasis Area and Severity Index, BW: body weight, BMI: body mass index, SNAQ: Simplified Nutritional Appetite Questionnaire, LDL: low-density lipoprotein, HDL: high-density lipoprotein, FBG: fasting blood glucose. Different superscripts (*, ‡) indicate statistically significant differences between the mean values in a row ($p<0.05$).

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Table 2. Comparison of clinical and laboratory data between the treatment subgroups

Clinical and laboratory findings	Treatment group/subgroup		Mean±SD	p
FBG difference (% change)	Conventional	Methotrexate	-5.24±17.98	0.470
		Acitretin	-0.41±9.35	
		Total	-3.7±15.40	
	Biologic	Anti-TNFα	-3.14±6.55	
		IL-17 inhibitor	3.61±11.82	
		Ixekizumab	112.9±42.30	
		Secukinumab	101.6±22.50	
		IL-12/23 inhibitor	0.29±11.53	
		IL-23 inhibitor	-2.22±17.63	
		Total	0.7±12.00	

SD: standard deviation, PASI: Psoriasis Area and Severity Index, BW: body weight, BMI: body mass index, SNAQ: Simplified Nutritional Appetite Questionnaire, LDL: low-density lipoprotein, HDL: high-density lipoprotein, FBG: fasting blood glucose. Different superscripts (*, ‡) indicate statistically significant differences between the mean values in a row ($p<0.05$).

Table 3. Relationship between obesity levels and changes in PASI, triglyceride, LDL, and HDL

		n	Mean±SD	p
PASI difference (% change)	<18.5	5	-87.17±17.32	0.758
	18.5-24.9	18	-53.88±84.86	
	25-29.9	34	-61.64±38.09	
	≥30	26	-63.22±70.13	
	Total	83	-61.99±60.37	
Triglyceride difference (% change)	<18.5	5	2.67±16.16	0.137
	18.5-24.9	18	22.86±56.46	
	25-29.9	33	7.71±37.39	
	≥30	25	-7.23±35.50	
	Total	81	6.15±41.81	
LDL difference (% change)	<18.5	5	1.72±35.57	0.161
	18.5-24.9	18	22.06±61.90	
	25-29.9	33	-1.57±20.70	
	≥30	24	1.23±27.45	
	Total	80	4.79±37.03	
HDL difference (% change)	<18.5	5	12.66±30.01	0.319
	18.5-24.9	18	-2.94±17.88	
	25-29.9	33	0.34±23.55	
	≥30	24	5.84±13.46	
	Total	80	2.02±20.25	
BMI difference (% change)	<18.5	5	-.35±3.70	0.291
	18.5-24.9	18	2.67±4.33	
	25-29.9	33	1.71±4.33	
	≥30	24	.71±3.12	
	Total	80	1.48±3.97	

SD: standard deviation, PASI: Psoriasis Area and Severity Index, LDL: low-density lipoprotein, HDL: high-density lipoprotein, BMI: body mass index

Table 4. Relationship between the SNAQ score and changes in BMI and PASI

		PASI difference (% change)
SNAQ score	r	-0.221
	p	**0.049**

SNAQ: Simplified Nutritional Appetite Questionnaire, BMI: body mass index, PASI: Psoriasis Area and Severity Index

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Table 5. Relationship between BMI difference (% change) and changes in the SNAQ score, waist circumference, and lipid profile

Clinical and laboratory parameters		BMI difference (% change)
SNAQ score	**r**	0.054
	p	0.637
Waist circumference difference (% change)	**r**	**0.397**
	p	**0.000**
Triglyceride difference (% change)	**r**	-0.142
	p	0.206
LDL difference (% change)	**r**	0.005
	p	0.968
Total cholesterol difference (% change)	**r**	-0.40
	p	0.727
HDL difference (% change)	**r**	-0.241
	p	0.085
FBG difference (% change)	**r**	0.038
	p	0.735
PASI difference (% change)	**r**	**-0.282**
	p	**0.01**

BMI: body mass index, SNAQ: Simplified Nutritional Appetite Questionnaire, LDL: low-density lipoprotein, HDL: high-density lipoprotein, FBG: fasting blood glucose, PASI: Psoriasis Area and Severity Index

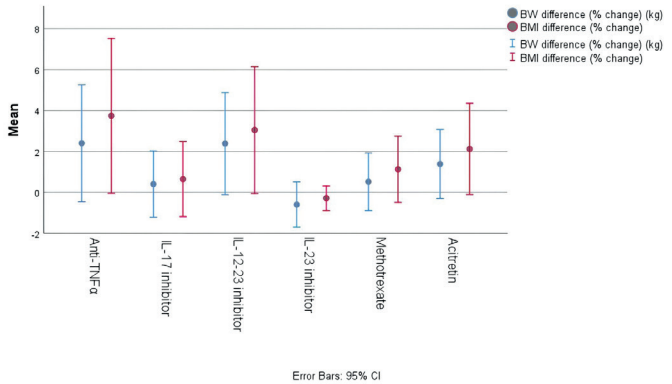

Figure 1. Comparison of body weight (BW) and body mass index (BMI) percent change rates between the treatment subgroups

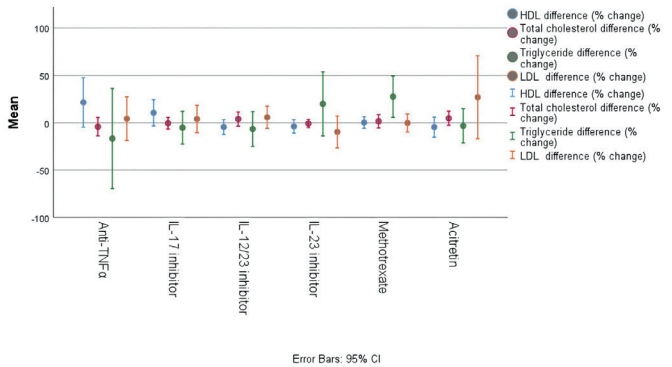

Figure 2. Comparison of blood lipid profile percent change rates between the treatment subgroups

Discussion

Obesity is associated with many important problems in patients with psoriasis. Cytokines such as TNFα, IL-6, resistin, adiponectin, leptin, and visfatin released from adipose tissue trigger psoriasis, exacerbate the existing disease and weaken the treatment response in these patients compared to normal-weight patients [7,12]. Considering that a 2.25 kg increase in body weight, even in healthy individuals, increases the risk of developing metabolic syndrome by 21-45%, it is clear that the presence of obesity in psoriasis patients will lead to significant increases in the risk of metabolic syndrome and cardiovascular disease [13]. In addition, the risk of depression is higher in obese patients, and the quality of life can be significantly affected in obese psoriasis cases. Furthermore, it has been shown that treatment discontinuation is more frequent in obese patients using anti-TNFα drugs, and BMI is an independent factor affecting treatment compliance [14,15].

It is known that there is a close relationship between TNFα and BW. TNFα suppresses adipogenesis by reducing anabolic hormones, such as insulin and insulin-like growth factor-1, stimulating lipolysis. It also induces protein catabolism in muscle tissue via NF-kappaB and increases overall proteolysis [16]. Thus, it reduces fat tissue and lean body mass by decreasing muscle tissue, thereby leading to weight loss [10]. TNFα also suppresses appetite by increasing leptin levels [11]. In the current study, we observed an increase of 2.40 kg in BW and 3.7% in BMI in patients using TNFα inhibitors, consistent with the literature [5]. Saraceno et al. evaluated weight gain in patients using anti-TNF α and MTX, and observed a weight gain of 1.54 kg with infliximab, 2.57 kg with adalimumab, and 2.18 kg with etanercept. Similar to our findings, no significant weight gain was observed in patients receiving MTX [17]. Briot et al. suggested that the weight gain in patients with spondyloarthropathy using anti-TNFα was mainly due to increased muscle mass and bone mineralization [18]. Renzo evaluated BMI and the SNAQ score in patients with psoriatic arthritis and psoriasis who were using infliximab and etanercept and found that these agents increased both lean body mass and adipose tissue by decreasing TNFα and IL-6 levels. But there was no change in their appetite [16]. In our study, we observed that waist circumference also increased in patients with an increased BMI. This finding demonstrates that anti-TNFα drugs cause an increase in adipose tissue. Although TNFα inhibition is theoretically expected to increase appetite by decreasing leptin levels, similar to Renzo et al., we detected no change in the patients' appetite using TNFα [16]. However, when we evaluated the correlation between the appetite scores and PASI, we found that patients with high appetite scores and high BMI values had a lower decrease in PASI.

It is known that increased inflammation secondary to TNFα raises plasma triglyceride levels and decreases HDL. By suppressing this inflammation with anti-TNFα drugs, it is expected to decrease triglyceride levels and an increase HDL levels. Although some studies have reported no change in triglyceride and cholesterol

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levels with etanercept, infliximab, and methotrexate treatments, we observed a decrease in triglyceride levels and a significant increase in HDL levels, as well as an increase in BW among patients using anti-TNFα [5,17].

IL-12/23 inhibition indirectly decreases TNFα levels. In addition, it has been shown that IL-12 and IL-23 are important cytokines involved in Th1 and Th17 cell activation. In addition, IL-17A plays a crucial role in developing metabolic syndrome in obese patients, inhibits adipogenesis, and increases leptin production, thereby reducing the risk of obesity [19].

There are conflicting reports on weight gain in patients receiving ustekinumab [11,20]. Gisondi et al. observed an increase of only 0.5 kg in patients taking ustekinumab [20]. In another study, a 28-week follow-up of 11 patients using ustekinumab revealed an increase of 2.27 kg in 64% of these patients [11]. In the PHOENIX study, the lipid profiles of patients were evaluated, and it was shown that ustekinumab had a neutral effect on cardiovascular parameters [21]. We observed an increase of 2.38 kg in patients using ustekinumab, an IL-12/23 inhibitor, similar to anti-TNFα. However, we did not detect significant changes in triglyceride or HDL levels. The PHOENIX 1 and PHOENIX 2 studies have shown that the response to ustekinumab is more limited in obese patients [22]. Therefore, in patients with psoriasis using ustekinumab, weight gain that will occur during the treatment process may increase treatment resistance, as well as the baseline BW.

We did not observe any changes in BW in patients using IL-17 inhibitors. While there was no change in the blood lipid profile in patients using secukinumab, we detected a significant increase of 24% in HDL levels using ixekizumab. In the UNCOVER-1, UNCOVER-2, and UNCOVER-3 studies, it was determined that ixekizumab had no effect on weight, did not change the blood lipid profile, including HDL, and had a neutral effect on the cardiovascular system [23]. Similarly, Takamura et al., who compared ustekinumab, secukinumab, and infliximab, found an increase in BW with the use of infliximab, despite no change among patients using ustekinumab and secukinumab [24]. The authors also noted that ustekinumab and secukinumab did not change the lipid profiles of patients [24].

In our study, we observed a decrease of 0.6 kg in patients using IL-23 inhibitors, although this was not statistically significant. We also observed a 19% increase in triglycerides and a 9.7% decrease in LDL, albeit with no statistically significant difference. To our knowledge, there is no study in the literature evaluated changes in BW in patients using IL-23 inhibitors. In light of the findings of the current study, IL-23 inhibitors present as promising treatment agents in obese and hypercholesterolemic patients because they provide weight loss and lead to positive changes in the blood lipid profile. Long-term studies with larger series are needed to clarify this effect.

Our study has some limitations, the most important being the small number of patients in drug subgroups. Our second important limitation is that 41 patients taking biologic drugs had previously used a different biologic. In addition, calorie intake and physical activity changes are known to be important confounding factors affecting changes in BW. Long-term studies with a large patient series of patients with and without systemic therapy, to evaluate calorie intake, physical activity, appetite monitoring, biometric changes, and bioimpedance analyses will yield more precise results for elucidating the effect of conventional and biologic drug treatments on BW, fat and lean muscle tissues, and the blood lipid profile.

Conclusion

In conclusion, while anti-TNFα and IL-12/23 inhibitors increase BW, IL-17 inhibitors and IL-23 inhibitors do not affect BW. Triglyceride levels increase with the use of MTX and decrease with the use of anti-TNFα or ixekizumab. Anti-TNFα and ixekizumab increase HDL levels. In the treatment of psoriasis, the presence of obesity and blood lipid profiles should be considered in the selection of the appropriate treatment for each patient.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
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Ethical Approval
This study was approved by the Non-Invasive Research Ethics Committee of Biruni University (2023/81-30).

References

1. Kisielnicka A, Szczerkowska-Dobosz A, Nowicki R. The influence of body weight of patients with chronic plaque psoriasis on biological treatment response. Postepy Dermatol Alergol. 2020;37:168-73.

2. Gürer MA. Introduction to psoriasis. Turkderm-Turk Arch Dermatol Venereol. 2016;50:2-3.

3. Sterry W, Strober B, Menter A, Council IP. Obesity in psoriasis: the metabolic, clinical and therapeutic implications. Report of an interdisciplinary conference and review. Br J Dermatol. 2007;157:649-55.

4. Herron MD, Hinckley M, Hoffman MS, et al. Impact of obesity and smoking on psoriasis presentation and management. Arch Dermatol. 2005;141:1527-34.

5. Gisondi P, Cotena C, Tessari G, Girolomoni G. Anti–tumour necrosis factor-α therapy increases body weight in patients with chronic plaque psoriasis: a retrospective cohort study. J Eur Acad Dermatol Venereol. 2008;22:341-4

6. Danielsen K, Wilsgaard T, Olsen AO, Furberg A-S. Overweight and weight gain predict psoriasis development in a population-based cohort. Acta Derm Venereol. 2017;97:332-9.

7. Kalkan G. Comorbidities in psoriasis: The recognition of psoriasis as a systemic disease and current management. Turkderm-Turk Arch Dermatol Venereology. 2017;51:71-7.

8. Snekvik I, Nilsen T, Romundstad P, Saunes M. Psoriasis and cardiovascular disease risk factors: the HUNT Study, Norway. J Eur Acad Dermatol Venereol. 2018;32:776-82.

9. Lorenz MW, Markus HS, Bots ML, et al. Prediction of clinical cardiovascular events with carotid intima-media thickness: a systematic review and meta-analysis. Circulation. 2007;115:459-67.

DOI: 10.5455/medscience.2023.07.113

10. Koutroubakis IE, Oustamanolakis P, Malliaraki N, et al. Effects of tumor necrosis factor alpha inhibition with infliximab on lipid levels and insulin resistance in patients with inflammatory bowel disease. Eur J Gastroenterol Hepatol. 2009;21:283-8.

11. Owczarczyk-Saczonek A, Placek W, Rybak-d'Obyrn J, Wygonowska E. Influence of ustekinumab on body weight of patients with psoriasis: an initial report. Postepy Dermatol Alergol. 2014;31:29-31.

12. Edson-Heredia E, Sterling KL, Alatorre CI, et al. Heterogeneity of response to biologic treatment: perspective for psoriasis. J Invest Dermatol. 2014;134:18-23.

13. Tan E, Baker C, Foley P. Weight gain and tumour necrosis factor-alpha inhibitors in patients with psoriasis. Australas J Dermatol. 2013;54:259-63.

14. Di Lernia V, Tasin L, Pellicano R, et al. Impact of body mass index on retention rates of anti-TNF-alfa drugs in daily practice for psoriasis. J Dermatolog Treat. 2012;23:404-9.

15. Naldi L, Addis A, Chimenti S, et al. Impact of body mass index and obesity on clinical response to systemic treatment for psoriasis. Evidence from the Psocare project. Dermatology. 2008;217:365-73.

16. Renzo LD, Saraceno R, Schipani C, et al. Prospective assessment of body weight and body composition changes in patients with psoriasis receiving anti-TNF-α treatment. Dermatol Ther. 2011;24:446-51.

17. Saraceno R, Schipani C, Mazzotta A, et al. Effect of anti-tumor necrosis factor-α therapies on body mass index in patients with psoriasis. Pharmacol Res. 2008;57:290-5.

18. Briot K, Garnero P, Le Henanff A, et al. Body weight, body composition, and bone turnover changes in patients with spondyloarthropathy receiving anti-tumour necrosis factor α treatment. Ann Rheum Dis. 2005;64:1137-40.

19. Endo Y, Yokote K, Nakayama T. The obesity-related pathology and Th17 cells. Cell Mol Life Sci. 2017;74:1231-45.

20. Gisondi P, Conti A, Galdo G, et al. Ustekinumab does not increase body mass index in patients with chronic plaque psoriasis: a prospective cohort study. Br J Dermatol. 2013;168:1124-7.

21. Reich K, Langley R, Lebwohl M, et al. Cardiovascular safety of ustekinumab in patients with moderate to severe psoriasis: results of integrated analyses of data from phase II and III clinical studies. Br J Dermatol. 2011;164:862-72.

22. Yanaba K, Umezawa Y, Ito T, et al. Impact of obesity on the efficacy of ustekinumab in Japanese patients with psoriasis: a retrospective cohort study of 111 patients. Arch Dermatol Res. 2014;306:921-5.

23. Egeberg A, Wu JJ, Korman N, et al. Ixekizumab treatment shows a neutral impact on cardiovascular parameters in patients with moderate-to-severe plaque psoriasis: Results from UNCOVER-1, UNCOVER-2, and UNCOVER-3. J Am Acad Dermatol. 2018;79:104-09.e8.

24. Takamura S, Takahashi A, Inoue Y, Teraki Y. Effects of tumor necrosis factor-α, interleukin-23 and interleukin-17A inhibitors on bodyweight and body mass index in patients with psoriasis. J Dermatol. 2018;45:1130-4.