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THERAPEUTIC HOTLINE

Prospective assessment of body weight and body composition changes in patients with psoriasis receiving anti-TNF-α treatment

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ABSTRACT: Tumor necrosis factor (TNF)-α is a pro-inflammatory cytokine associated with psoriasis pathogenesis. Anti-TNF-α therapies are effective in psoriasis. A significant weight gain has been reported in patients treated with anti-TNF-α agents. The aim of the present study was to evaluate the body composition changes in psoriatic patients receiving anti-TNF-α therapies according with disease phenotype. Forty patients affected with psoriasis were followed up for 24 weeks and divided into two groups: psoriasis vulgaris (PsO) and psoriatic arthritis (PsA). Anthropometric, blood biochemical, body composition parameters, resting metabolic rate, and disease activity indexes were measured at baseline and at week 24. After 24 weeks of anti-TNF-α administration, the disease activity indexes and concentration of inflammatory markers were significantly decreased. Seventy-five percent of PsO and 60% of PsA patients had an increase in body weight. Weight changes correlated with fat mass gain in the PsO group, and with fat and lean mass gain in the PsA group. In the present study, we demonstrated that a blockage of TNF-α bioactivity is related with fat and lean mass gain in both PsO and PsA subjects. The anti-TNF-α therapies could play a key role in the cross talk between adipose tissue and skeletal muscle, mediated by the reduction of TNF-α and interleukin-6 production.

KEYWORDS: biologics, body composition, psoriasis

Introduction

Psoriasis is a chronic inflammatory skin and joints disease associated with an increased expression of tumor necrosis factor (TNF)-α (1). The latter induces muscle loss stimulating muscle protein breakdown and down regulating the expression of

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anabolic hormones and growth factors (2). According with the multiple systemic effects of TNF-α, the TNF-α antagonists could be associated with a weight gain due to an increase in the fat-free mass. Etanercept and infliximab are anti-TNF-α molecules effective in the treatment of psoriasis (PsO) and psoriatic arthritis (PsA) (3).

We have previously shown that a significant weight gain occurred in psoriatic patients under treatment with anti-TNF-α agents (4). In order to evaluate if the increase in weight was due to an increase in fat-free mass, we performed a prospective study measuring the changes in body composition in patients with psoriasis receiving anti-TNF-α therapies.

Materials and methods

An open prospective 24-week study was performed in patients receiving infliximab (Remicade®, Shering-Plough S.P.A / Merck & Co., Inc., Whitehouse Station, NJ) or etanercept (Enbrel®, Wyeth Lederle S.P.A./Pfizer Italia) for the treatment of psoriasis. The study was approved by the local ethical committee, and all patients provided a written consent.

Patients were excluded if they had previously received biologics, had an associated endocrinological disorder, were under diet or intense physical training, or did not conclude the 24 weeks of treatment. Severity of the disease was assessed by Psoriasis Area and Severity Index (PASI) and the Disease Activity Score (DAS)-28. At each visit, assessment of anthropometric measures, body mass index (BMI), body composition by Dual-X absorptiometry (DXA), resting metabolic rate (RMR), and standard serum laboratory tests, was performed according to previously described procedures (5). Data on diet, physical activity (PA), and changes in appetite (Simplified Nutritional Appetite Questionnaire – SNAQ) were collected (6). Patients were evaluated at baseline and at week 24.

Plasma concentrations of TNF-α and interleukin-6 (IL-6) were determined in duplicate using a high-sensitivity commercial sandwich enzyme-linked immunosorbent assay kit (Mactech AB, Nacka, Sweden).

Statistical analysis

Data analysis was performed on the total study population (total group) and on psoriatic patients divided in PsO and PsA. Kolmogorov–Smirnov test, paired samples *t*-test and Wilcoxon test and Pearson correlation were performed using SPSS11.01 Software (SPSS for Windows, Rel. 11.0.1. 2001, SPSS Inc., Chicago, IL).

Results

Among 61 subjects recruited for the study, 15 were excluded at the screening and six were withdrawn for missing data in any variables considered. Patients were divided into two groups: 20 patients with PsO and 20 with PsA. Baseline characteristics of the study population are listed in Table 1. Twelve patients received infliximab and 28 received etanercept.

Anthropometric parameters and body composition features at baseline and at week 24 are given in Tables 2 and 3. After 24 weeks, a significant increase in body weight and BMI was observed in both, PsO and PsA (FIG. 1, Table 2). The weight gain was 2.6% ± 3.2% and 2.1% ± 3.5%, in the PsO and

Table 1. Baseline characteristics of the study population[a]

Parameters	PsO group ($n = 20$)	PsA group ($n = 20$)
Age (years)	36.8 ± 8.4	42.2 ± 8.9
Smokers (%)	75	60
SNAQ (score)	14.5 ± 1.3	15.3 ± 1.4
RMR (Kcal/day)	1782.9 ± 248.3	1815.9 ± 332.3
VO_2 (L/minute)	0.3 ± 0.1	0.3 ± 0.1
VCO_2 (L/minute)	0.2 ± 0.1	0.2 ± 0.1
RR	0.9 ± 0.1	0.9 ± 0.1
PASI	12.4 ± 8.1	7.6 ± 6.5
Disease duration (years)	15.0 ± 9.3	14.1 ± 11.2
Familiarity (%)	70	65

[a]Age, SNAQ, RMR, VO2,VCO2, RR, PASI, and disease duration are indicated as arithmetic $\bar{x} \pm$ SD.

PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; PsO, psoriasis vulgaris; RMR, resting metabolic rate; RR, respiratory ratio (VCO_2/VO_2); VCO_2, carbon dioxide production; VO_2, oxygen consumption.

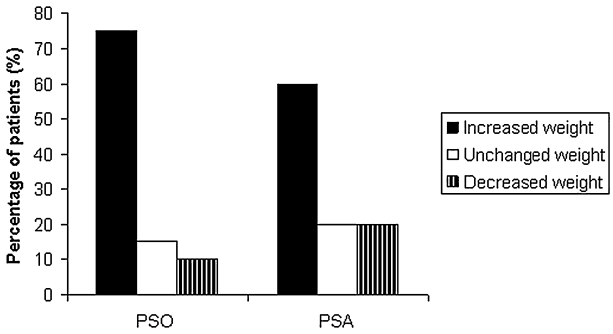

FIG. 1. Body weight changes in PsO and PsA patients after anti-TNF-α therapy. Each group was subdivided depending on the percentage of patients with increased, unchanged, and decreased weight, with respect to the baseline (PsO: *n* = 20; PsA: *n* = 20).

PsA group, respectively; significant differences in waist and waist/hip ratio were observed in the total group after treatment (Table 2). The body composition evaluation, showed significant differences after treatments. Gain in total lean and fat mass, according with disease phenotype and anatomical regions, are showed and reported in FIG. 2 and Table 3. In both groups, a significant percent change of body weight, fat, and lean mass, compared to the baseline (PsO: body weight +3.8 ± 2.5%, fat mass 8.6 ± 10.5%, lean mass 1.9 ± 2.4%; PsA: body weight +3.7 ± 3.4%, fat mass 8.9 ± 17.3%, lean mass 2.9 ± 3.4%) was observed. No remark-

Table 2. Anthropometric parameters of total, PsO and PsA patients, at baseline and 24 weeks after anti-TNF-α therapy[a]

	Total group (*n* = 40)		PsO group (*n* = 20)		PsA group (*n* = 20)	
Parameters	Baseline	Week 24	Baseline	Week 24	Baseline	Week 24
Weight (kg)	83.93 ± 14.41	85.82 ± 14.40[d]	85.41 ± 14.32	87.64 ± 14.13[d]	82.43 ± 14.75	84.06 ± 14.92[c]
BMI (kg/m^2)	27.61 ± 4.32	28.35 ± 4.42[d]	28.23 ± 4.8	28.95 ± 4.71[d]	27.11 ± 3.93	27.61 ± 4.03[c]
Waist (cm)	93.60 ± 15.01	96.22 ± 11.30[b]	96.64 ± 11.61	97.92 ± 11.34	90.71 ± 17.64	94.53 ± 11.32
Hip (cm)	99.90 ± 13.33	102.32 ± 7.62	102.22 ± 8.94	103.43 ± 8.92	97.71 ± 16.43	101.13 ± 6.12
W/H	0.93 ± 0.07	0.94 ± 0.07[b]	0.94 ± 0.07	0.95 ± 0.07	0.92 ± 0.07	0.93 ± 0.08

[a]All values are arithmetic $\bar{x}$ ± SD.
[b]Reflects the significance of the differences within groups between baseline and week 24 determined with a paired *t*-test ($p \leq 0.05$).
[c]Reflects the significance of the differences within groups between baseline and week 24 determined with a paired *t*-test ($p \leq 0.01$)
[d]Reflects the significance of the differences within groups between baseline and week 24 determined with a paired *t*-test ($p \leq 0.001$).
BMI, body mass index; PsA, psoriatic arthritis; PsO, psoriasis vulgaris; W/H, waist/hip.

Table 3. Body composition parameters by DXA (Dual energy X-ray Absorptiometry) of total, PsO and PsA patients, at baseline and 24 weeks after anti-TNF-α therapy[a]

	Total group (*n* = 40)		PsO group (*n* = 20)		PsA group (*n* = 20)	
Parameters	Baseline	Week 24	Baseline	Week 24	Baseline	Week 24
FM (kg)	26.1 ± 9.3	27.4 ± 9.4[c]	27.3 ± 10.4	28.9 ± 10.5[c]	24.9 ± 8.2	25.8 ± 7.6
FM (%)	31.4 ± 7.5	32.3 ± 6.7[b]	31.7 ± 8.4	33.3 ± 7.9[b]	31.1 ± 6.6	31.3 ± 5.3
FM trunk (kg)	16.2 ± 6.2	16.8 ± 5.9[b]	17.1 ± 6.8	17.7 ± 6.7[b]	15.3 ± 5.5	15.9 ± 5.1
FM arms (kg)	2.1 ± 0.8	2.3 ± 0.9[d]	2.1 ± 0.8	2.4 ± 0.9[b]	2.0 ± 0.8	2.3 ± 0.8[b]
FM legs (kg)	7.0 ± 2.8	7.4 ± 2.8[c]	7.3 ± 3.2	7.9 ± 3.3[c]	6.8 ± 2.3	7.0 ± 2.2
FM L2-L5 (kg)	3.6 ± 1.6	3.8 ± 1.7	3.9 ± 1.7	4.1 ± 2.0	3.4 ± 1.5	3.5 ± 1.4
LM (kg)	54.4 ± 6.9	55.0 ± 6.9[b]	54.9 ± 5.3	55.3 ± 5.4	53.8 ± 8.3	54.6 ± 8.5
LM (%)	68.4 ± 7.6	68.0 ± 8.1	67.9 ± 8.5	67.7 ± 10.2	69.0 ± 6.8	68.4 ± 5.5
LM trunk (kg)	25.9 ± 3.9	26.3 ± 3.6	26.3 ± 3.3	26.4 ± 3.0	25.4 ± 4.5	26.1 ± 4.2
LM arms (kg)	7.4 ± 2.9	7.7 ± 2.9[c]	7.7 ± 3.5	8.0 ± 3.6[b]	7.1 ± 2.3	7.3 ± 2.0
LM legs (kg)	17.2 ± 4.3	17.3 ± 4.3	17.1 ± 4.4	17.3 ± 4.4	17.2 ± 4.3	17.4 ± 4.4
LM L2-L5 (kg)	5.0 ± 1.1	5.1 ± 1.0	5.2 ± 0.8	5.1 ± 0.9	4.9 ± 1.4	5.1 ± 1.2

[a]All values are arithmetic $\bar{x}$ ± SD.
[b]Reflects the significance of the differences within groups between baseline and week 24 determined with a paired *t*-test ($p \leq 0.05$).
[c]Reflects the significance of the differences within groups between baseline and week 24 determined with a paired *t*-test ($p \leq 0.01$).
[d]Reflects the significance of the differences within groups between baseline and week 24 determined with a paired *t*-test ($p \leq 0.001$).
FM, fat mass; LM, lean mass; LM L2-L5, lean mass from L2 to L5 vertebral disc space; PsA, psoriatic arthritis; PsO, psoriasis vulgaris.

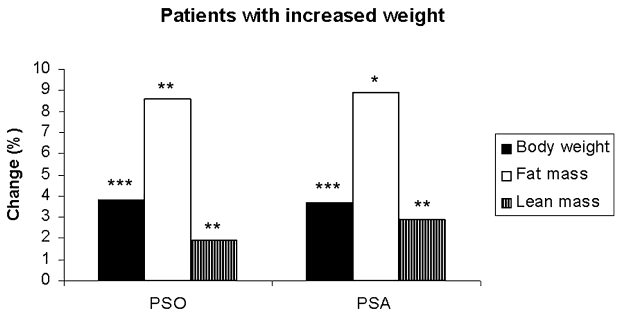

FIG. 2. Relative changes (%) in fat and lean mass, in PsO and PsA patients with increased weight, after anti-TNF-α therapy, with respect to the baseline. The values are expressed as means of relative changes. *Reflects the significance of the differences within groups between baseline (T0) and week 24 (T1) determined with a paired *t*-test ($p \leq 0.05$). **Reflects the significance of the differences within groups between baseline (T0) and week 24 (T1) determined with a paired *t*-test ($p \leq 0.01$). ***Reflects the significance of the differences within groups between baseline (T0) and week 24 (T1) determined with a paired *t*-test ($p \leq 0.001$; PsO: $n = 20$; PsA: $n = 20$).

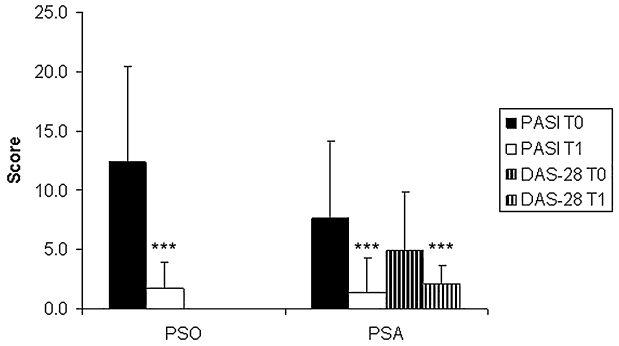

FIG. 3. Psoriasis Area and Severity Index (PASI) and Disease Activity (DAS-28) scores of PsO and PsA patients before and after anti-TNF-α therapy. ***Reflects the significance of the differences within groups between baseline (T0) and week 24 (T1) determined with a paired *t*-test ($p \leq 0.001$; PsO: $n = 20$; PsA: $n = 20$).

able differences in body composition changes between PsO and PsA groups were found.

After 24 weeks of therapy, a significant clinical improvement assessed by PASI and DAS-28 scores was observed in each group (FIG. 3).

Changes in physical activities, appetite, smoking habits, diet, RMR, and biochemical parameters were not highlighted during treatments.

In contrast, a significant decrease in systemic inflammation assessed by the erythrocyte sedimentation rate (ESR) was observed in both groups (PsA: 17.3 ± 17.8 vs. 6.5 ± 4.2, $p \leq 0.05$; PsO: 16.2 ± 17.2 vs. 7.0 ± 5.7, $p \leq 0.05$).

The variation in TNF-α and IL-6 serum concentration after 24 weeks of therapy are represented in

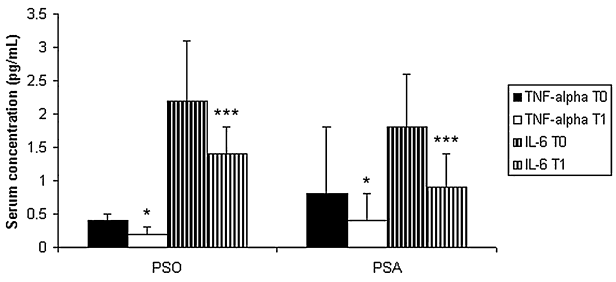

FIG. 4. TNF-α and IL-6 serum concentration of PsO and PsA patients before and after anti-TNF-α therapy. *Reflects the significance of the differences within groups between baseline (T0) and week 24 (T1) determined with a Wilcoxon test ($p \leq 0.05$). ***Reflects the significance of the differences within groups between baseline (T0) and week 24 (T1) determined with a Wilcoxon test ($p \leq 0.001$; PsO: $n = 20$; PsA: $n = 20$).

FIG. 4. A significant decrease in TNF-α and IL-6 serum concentration was highlighted in both PsO and PsA (respectively T0: 2.2 ± 0.9; T1: 1.4 ± 0.9, $p \leq 0.001$; T0: 1.8 ± 0.8; T1: 0.9 ± 0.5, $p \leq 0.001$).

Pearson correlation analysis showed that in the PsO group, there was a significant negative correlation between % change of PASI and weight (R: –0.77; $p \leq 0.001$) and between percent change of PASI and fat mass (R: –0.78; $p \leq 0.001$; Table 4). In the PsA group, there was a significant correlation between percent change of weight and IL-6 (R: –0.40; $p \leq 0.05$); percent change of weight and DAS-28 (R: –0.38; $p \leq 0.05$); percent change of weight and ESR (R: 0.42; $p \leq 0.05$). Furthermore, remarkable was the correlation between percent change of lean mass, IL-6 (R: –0.40; $p \leq 0.05$), DAS-28 (R: –0.62; $p \leq 0.001$), and ESR (R: 0.46; $p \leq 0.05$).

Discussion

We have previously reported that a significant weight gain occurred in patients treated with anti-TNF-α agents (4). Since psoriasis is a systemic disease associated with cardiovascular and metabolic comorbidities (7), to clarify if the changes in weight and BMI are due to an increase in the fat or in the lean mass was considered crucial.

We found that the anti-TNF-α drugs were related with changes in body composition, in both PsO and PsA subjects. Seventy-five percent of PsO patients and 60% of PsA patients showed an increase in body weight and a significant gain in the total fat and lean mass after anti-TNF-α therapies. In the weight gain population of PsO patients, the variation of fat and lean mass was 8.6% and 1.9%, respectively; whereas in the PsA patients, the

Table 4. Pearson correlation analysis of 24 weeks changes of body composition and inflammatory parameters, in PsO and PsA groups[a]

	PsO group ($n = 20$)			PsA group ($n = 20$)		
% change	Weight	FM	LM	Weight	FM	LM
TNF-α	–0.37	–0.36	0.16	0.12	–0.03	0.18
IL-6	0.18	0.23	0.33	–0.40[b]	0.21	–0.40[b]
PASI	–0.77[c]	–0.78[c]	–0.10	–0.21	–0.04	–0.24
DAS-28	ND	ND	ND	–0.38[b]	0.16	–0.62[c]
ESR	0.31	0.15	0.25	0.42[b]	0.31	0.46[b]
CRP	–0.17	–0.15	–0.22	–0.31	–0.32	0.15
Weight	1	0.97[c]	0.10	1	0.70[c]	0.60[c]
FM	0.97[c]	1	–0.09	0.70[c]	1	–0.08
LM	0.10	–0.09	1	0.60[c]	–0.08	1

[a]All values are Pearson correlation coefficients.
[b]Reflects the significance of correlation between variables determined with a Pearson correlation analysis ($p \leq 0.05$).
[c]Reflects the significance of correlation between variables determined with a Pearson correlation analysis ($p \leq 0.001$).
CRP, C-reactive protein; DAS-28, Disease Activity Score; ESR, erythrocyte sedimentation rate; FM, fat mass; IL-6, interleukin-6; LM, lean mass; ND, not determined; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; PsO, psoriasis vulgaris; TNF-α, tumor necrosis factor-α.

increase in fat and lean mass was 8.9% and 2.9%, respectively. This observation is consistent with studies performed in other chronic illnesses, such as spondyloarthropathy and Crohn's disease (8,9).

A significant reduction in TNF-α and IL-6 circulating amount was observed in the two groups (FIG. 4) and a significant correlation was found between percentage of changes of weight and inflammatory parameters. In the PsA group, the increase in weight and lean mass was associated with a higher reduction in IL-6 amount, as shown by the correlation analysis (Table 4). This observation underlines the link between body composition changes in terms of adipose tissue, muscle metabolism, and cytokine profile (10). Evidence of this comes from the multiple systemic effects of TNF-α that is involved in body weight homeostasis by increasing lipolysis, favoring muscle cell catabolism and stimulating general proteolysis by increasing ubiquitin conjugation to muscle proteins via an NF-kappaB-dependent process (11–17). According with the aforementioned activities, the anti-TNF-α therapies can be associated with a weight gain due to an increase in the fat and lean mass.

To our knowledge, this is the first study reporting an evaluation of body composition in psoriatic patients under treatment with anti-TNF-α agents. The increase in fat mass could have significant implication in clinical practice in terms of augmented risk of obesity-related chronic degenerative diseases (18,19). In contrast, the increase in lean mass could represent a benefit since muscle represents the protein reserve of the body inducing an improved immune function.

In conclusion, anti-TNF α therapies could play a crucial role in the cross talk between adipose tissue and skeletal muscle, mediated by the reduction of TNF-α and IL-6 production.

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