JEADV ISSN 1468-3083

ORIGINAL ARTICLE

Anti–tumour necrosis factor-α therapy increases body weight in patients with chronic plaque psoriasis: a retrospective cohort study

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Keywords
anti-TNF-alpha therapy, body weight, chronic plaque psoriasis

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Received: 16 April 2007,
accepted 26 June 2007

DOI: 10.1111/j.1468-3083.2007.02429.x

Abstract

Background Chronic plaque psoriasis is associated with overweight or obesity. Anti–tumour necrosis factor-α (anti-TNF-α) treatments are now frequently used in psoriasis management. TNF-α is deeply involved in body weight homeostasis, which may be affected by TNF-α–targeted therapy.

Objective To investigate whether anti-TNF-α treatments is associated with changes in body weight in patients with chronic plaque psoriasis.

Methods We performed a retrospective controlled analysis comparing the variations in body weight and body mass index (BMI) in three closed cohorts of psoriatic patients during a 6-month treatment with etanercept ($N = 58$), infliximab ($N = 40$) or methotrexate ($N = 43$).

Results We observed a body weight increment of 1.5 ± 2.7 kg (mean ± SD; $P = 0.0002$) and 2.5 ± 3.3 kg ($P = 0.004$) in patients treated with etanercept and infliximab, respectively. In contrast, a non-significant change (0.6 ± 1.4 kg; $P = 0.4$) was measured in patients treated with methotrexate. The BMI increased with 0.5 ± 0.5 ($P = 0.01$) and 0.8 ± 1 ($P = 0.003$) points in patients treated with etanercept and infliximab, respectively, whereas it did not change (< 0.2 ± 0.5; $P = 0.06$) in patients treated with methotrexate. About one fourth of patients experienced a 4- to 10-kg weight gain. Differences in body weight variations among patients treated with anti-TNF-α therapies and methotrexate were statistically significant ($P = 0.0005$). We could not identify clinical parameters predicting this phenomenon.

Conclusions Patients with psoriasis treated with long-term anti-TNF-α therapies may manifest a body weight gain. This effect should be taken into account in the global approach to patients with psoriasis.

Introduction

Chronic plaque psoriasis is associated with obesity in 12.9% to 34% of cases.[1–4] Although the directionality of this positive correlation is still unclear, two studies suggest that overweight and obesity appear after the onset of psoriasis.[1,5] In contrast, two other studies found a high prevalence of obesity in patients with recent onset psoriasis, suggesting that obesity precedes and may represent a risk factor for psoriasis.[2,6] Obesity is a strong risk factor for hypertension and type 2 diabetes, and all of these are important cardiovascular risk factors. Indeed, it has been documented that there is an increased mortality from cardiovascular diseases in patients with severe psoriasis, and psoriasis may confer an independent risk of myocardial infarction especially in young patients.[7,8] Anti–tumour necrosis factor-α (anti-TNF-α) treatments are now frequently used in psoriasis management. TNF-α is deeply involved in body weight homeostasis, which may be affected by TNF-α–targeted therapy. Recently, body

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weight gain has been reported both in patients with spondyloarthropathy[9] and patients with Crohn's disease[10] treated with anti-TNF-α inhibitors. We conducted a retrospective cohort study aimed to see whether anti-TNF-α treatments are associated with changes in body weight in patients with psoriasis.

Materials and methods

Study population

One hundred and forty-one psoriatic patients consecutively admitted to the outpatients clinics of the University Hospital of Verona were involved. The source population of the study was people living in city of Verona or in the neighbourhood. Patients were affected by chronic plaque psoriasis diagnosed according to clinical criteria. Patients with psoriatic arthritis diagnosed according to the CASPAR criteria were excluded.[11] All subjects were visited by a dermatologist who registered demographical, biometrical and the other relevant data on a case report form. Visits were scheduled at baseline and every 2 months for patients treated with methotrexate and etanercept, whereas visits were scheduled at each infusion for patients receiving infliximab. Relevant data collected included age, gender, weight, height, body mass index (BMI), age of psoriasis onset, type and severity of psoriasis and concomitant medications. BMI was calculated as weight (kg)/height (cm^2). Severity of psoriasis was assessed according to the Psoriasis Area and Severity Index (PASI) and body surface area (BSA). Venous samples were taken at baseline visit and every 2 months after the subjects had fastened overnight (at least 8 h). Patients were treated with methotrexate, etanercept or infliximab, respectively. The indications for anti-TNF-α treatments were chronic plaque psoriasis with a PASI score and a BSA% involvement of more than 10 and resistance or intolerance to methotrexate, cyclosporin, acitretin or phototherapy. Etanercept and infliximab were randomly assigned to patients resistant or intolerant to methotrexate, which was used as the first choice drug. All patients who received etanercept or infliximab were biological therapy naïve. Doses of systemic drugs used were as follows: methotrexate was given 15 mg once weekly by intramuscular injection; etanercept 25 mg twice weekly by subcutaneous injections; and infliximab 5 mg/kg at week 0, 2, 6 and then every 8 weeks by intravenous infusion.

Statistical analysis

Analysis was made using the STATA (version 6.0 StataCorp LP, College Station, TX, USA) and Graphpad (version 4.0 GraphPad Software, El Camino Real, San Diego, CA, USA) software packages. Standard descriptive statistics, such as mean and standard deviation, were computed. Differences in body weight, BMI, PASI score, plasma glucose, total cholesterol and triglycerides within groups were compared using Wilcoxon's signed rank sum test. Differences between groups were compared using ANOVA test corrected using the Bonferroni formula. Associations between body weight increment and categorical variables (age and gender) were tested by Fisher exact test, whereas *t*-test was used for continuous variables (BMI, body weight, PASI score and serum lipids). All *P*-values are two sided, and $P < 0.05$ was considered statistically significant.

Results

Forty-three patients treated with methotrexate, 58 patients with etanercept and 40 patients with infliximab were included in the study (Table 1). At enrolment, no significant differences in age, sex, body weight and BMI were present among the three groups of patients. Psoriasis duration was also similar in the three groups, whereas patients treated with methotrexate had a lower PASI score. At 6 months, we observed a mean body weight increment of 1.5 ± 2.7 kg (± SD; $P = 0.0002$) and 2.5 ± 3.3 kg ($P = 0.004$) in patients treated with etanercept and infliximab, respectively. In contrast, a non-significant change (–0.6 ± 1.4 kg; $P = 0.4$) was measured in patients treated with methotrexate. In particular, in the etanercept cohort, 6 patients (10.3%) lose weight; 15 patients (25.8%) did not show body weight variation; 24 patients (41.3%) increased weight by 1 to 3 kg; and 13 patients (22.4%) increased weight by 4 to 10 kg. In the cohort of infliximab, 3 patients (7.5%) lose weight, 7 (17.5%) did not show body weight change; 19 patients (47.5%) increased weight by 1 to 3 kg; and 11 patients (27.5%) increased weight by 4 to 10 kg. In the methotrexate cohort, 8 patienta (18.6%) lose weight; 32 patients (74.4%) did not show body weight variation; and 3 patients (6.9%) increased weight by 1 to 3 kg. The BMI increased with 0.5 ± 0.5 (mean ± SD; $P = 0.01$) and 0.8 ± 1 ($P = 0.003$) points in patients treated with etanercept and infliximab, respectively, whereas it did not change (–0.2 ± 0.5; $P = 0.06$) in patients treated with methotrexate. Differences in body weight variations among patients treated with anti-TNF-α therapies and methotrexate were statistically significant ($P = 0.0005$). The relative risk of gaining ≥ 5 kg of body weight among patients exposed to anti-TNF-α treatments was 4.3 times higher than in patients exposed to methotrexate. There were no differences in body weight mean increment according to age group (> 50 or < 50 years old), gender, BMI classes and psoriasis severity (PASI score > 10 or < 10) at enrolment. After 6 months of treatment, mean PASI score was decreased by 47.1% ($P = 0.0002$), 74.5%

Table 1 Study population. Descriptive characteristic of the three groups of patients

	MTX	Δwithin group*	Etanercept	Δwithin group*	Infliximab	Δwithin group*	Δbetween groups†
Number	43		58		40		
Sex, F/M	17/26		19/39		12/28		0.5
Age (y), mean ± SD	53.1 ± 12.7		50.2 ± 11.1		46.8 ± 11.2		0.7
Psoriasis duration (y), mean ± SD	18.6 ± 12		22 ± 12.9		17.5 ± 13.4		0.2
Body weight at enrolment, mean ± SD	81.0 ± 12.6		80.1 ± 16.2		79.2 ± 15.2		0.9
Body weight at month 6, mean ± SD	79.2 ± 13.9	0.4	81.7 ± 16.4	0.0002	81.8 ± 16.9	0.004	0.6
BMI at enrolment, mean ± SD	27.4 ± 3.6		27.6 ± 5		26.5 ± 3.5		0.6
BMI at month 6, mean ± SD	27.3 ± 3.8	0.06	28.1 ± 5	0.01	27.3 ± 3.8	0.003	0.7
PASI at enrolment, mean ± SD	8.2 ± 3.1		18.8 ± 7.4		17.7 ± 7.3		0.0001‡; 0.6§
PASI at month 6, mean ± SD	4.3 ± 6	0.0002	4.8 ± 4.7	0.0001	2.1 ± 3.2	0.0001	
PASI mean improvement percentage	47.6		74.5		88.8		0.0004‡; 0.02§
Total cholesterol level at enrolment, mean ± SD	234 ± 16.8		233 ± 15.1		235.3 ± 14.2		0.8‡; 0.7§
Total cholesterol level at month 6, mean ± SD	236 ± 18.1	0.4	235 ± 17.3	0.5	237 ± 16.9	0.6	
Triglycerides levels at enrolment, mean ± SD	170 ± 17.8		168 ± 18.3		172 ± 18.1		
Triglycerides levels at month 6, mean ± SD	175 ± 18.9	0.2	167 ± 19.4	0.7	170 ± 16.2	0.09	

*Differences within groups were compared using Wilcoxon's signed rank sum test;
†Differences between groups were compared using ANOVA test corrected using Bonferroni formula;
‡Methotrexate vs. etanercept or infliximab;
§Etanercept vs. infliximab.
MTX, methotrexate.

($P = 0.0001$) and 88.8% ($P = 0.0001$) in patients treated with methotrexate, etanercept and infliximab, respectively. No significant changes in fasting plasma glucose, total cholesterol and triglycerides mean levels were observed in any of the three groups as well as no severe adverse events.

Discussion

These data show that patients with psoriasis receiving anti-TNF-α therapy, but not those treated with methotrexate, may manifest a significant body weight gain after 6 months of treatment. A relevant increase (4–10 kg) in body weight was observed in about 25% of patients treated with etanercept or infliximab. We could not identify clinical parameters predicting this phenomenon. No patients referred modifications in eating behaviour and physical activity and/or increment of appetite or anorexia. We did not study body composition by bioimpedance, whereas Briot *et al*. reported an increase in body weight, bone mineral density and in lean mass, but not in fat mass, in parallel with an increase in insulin-like growth factor-1 in patients with spondyloarthropathies (including psoriatic arthritis) receiving a 1-year anti-TNF-α treatment.[9] In contrast, no studies have reported body weight gain in patients with rheumatoid arthritis after anti-TNF-α therapy. Therefore, it is possible that the different type of inflammation/immune response or the genetic background (usually patients with rheumatoid arthritis are lean) is important in determining whether anti-TNF-α can favour weight gain. Our study has several limitations, including the possible selection of the more severe psoriatic patients in the anti-TNF-α–treated group. Although baseline PASI scores were not significantly different in the three groups, etanercept and infliximab were randomly assigned to patients resistant or intolerant to methotrexate or other traditional systemic therapies, which were used as the first-line therapy.

The reason for the increased weight among patients treated with anti-TNF-α agents is not known. TNF-α/cachectin α is deeply involved in body weight homeostasis by favouring muscle cell catabolism both in physiological and pathological conditions.[12–14] Anti-TNF-α treatment may have and indirect positive effect on lean mass throughout the general health improvement of patients, leading to increase of appetite. Indeed, TNF-α can influence appetite through modulation of leptin release from adipocytes.[15] Franchimont *et al*. observed that a 4-week infliximab treatment induced a body weight and an increase in leptin serum levels in patients with Crohn's disease.[10] We did not observe differences in plasma triglycerides and cholesterol levels following any treatments, although significant elevation in plasma lipids have been reported in some patients with rheumatoid arthritis or psoriasis treated with TNF-α inhibitors.[16,17] On the other hand, recent reports suggest TNF-α inhibitors can improve

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metabolic parameters and reduce cardiovascular risk factors. In particular, TNF-α blockade has been shown to improve insulin resistance, reduce serum levels of C-reactive protein and carotid intima-media thickness in patients with rheumatoid arthritis.[18,19]

The potential effect of anti-TNF-α treatments on body weight should be taken into account in the long-term their use in overweight and obese psoriatic patients.

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