Effectiveness of Systemic Therapies in Patients with Obesity and Psoriasis: A Single-center Retrospective Study

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ABSTRACT This retrospective study included 63 patients with obesity (Body Mass Index; BMI ≥ 30) and psoriasis. Our aim was to verify the effectiveness of different systemic therapies administered to the above cohort of subjects over a period of 1 year. Improvements of 75%, 90%. and 100% compared with the baseline Psoriasis Area Severity Index (PASI 75, PASI 90, and PASI 100, respectively) were used as clinical outcome measures. In a median time of 16 weeks, 85.7%, 68.2%, and 38.0% of patients achieved PASI 75, PASI 90, and PASI 100, respectively. In parallel, the Dermatology Life Quality Index (DLQI) and the visual analog score for measuring itch intensity (VAS itch) decreased significantly ($P<0.0001$ for both parameters). At the achievement of PASI 75, BMI increased as compared to baseline *(P=0.02)* and did not significantly vary at the attainment of PASI 90 and PASI 100 (*P*= 0.07 for both outcomes). Logistic multivariate regression analysis showed that treatment with biologic drugs was a positive predictor for achieving PASI 75, PASI 90, and PASI 100. BMI >31.7 and the presence of psoriatic arthritis were negative predictors for the achievement of PASI 90, while having a DLQI >6 was a positive predictor.

KEY WORDS: psoriasis, obesity, therapy

INTRODUCTION

Psoriasis is a common debilitating disease often associated with several comorbidities. Obesity is one of the most frequent among them (1). Interestingly, epidemiological data indicate a bidirectional relationship between psoriasis and obesity. In particular, an increased frequency of obesity in the psoriatic population corresponds to an increased risk of developing psoriasis in subjects with obesity (2).

The coexistence of obesity with psoriasis poses several problems in the management of the latter disease. In fact, obesity contributes towards increasing the frequency of several diseases often associated with psoriasis, such as major cardiovascular events, non-alcoholic fatty liver disease (NALFD), dyslipidemia, metabolic syndrome, and hypertension (3). These comorbidities need to be taken into account in the choice of systemic therapy because they can be promoted or exacerbated by different drugs used in psoriasis (e.g., hepatotoxicity of methotrexate, hypertensive effect of cyclosporine, increased triglycerides and/or cholesterol blood levels from acitretin, and increased body weight from tumor necrosis factor inhibitors).

Another important aspect to consider is that obesity is associated with a decrease in the effectiveness of several antipsoriatic synthetic or biologic drugs (1) as well as their reduced survival (1,4).

Although the negative effects of obesity on the management of psoriasis have been reported (1), data are rather controversial (5-10). Moreover, only a few studies have been specifically designed to evaluate the effect of systemic therapies in patients with obesity and psoriasis who did not receive any active intervention such as diet restrictions and/or a program of structured physical exercise (5).

This study aimed to evaluate the frequency with which a cohort of patients with obesity and psoriasis , retrospectively evaluated, achieved an effective therapeutic response after starting a systemic therapy. No patients received active interventions for body weight reduction, apart from generic information on the usefulness of reducing weight to improve the clinical control of psoriasis.

PATIENTS AND METHODS

Study design

This was a retrospective study to assess the proportion of patients with obesity (Body Mass Index; BMI ≥30) and psoriasis who achieved a therapeutic response over 1 year of systemic therapy. The Psoriasis Area and Severity Index (PASI; range 0-72) (11) was used to score the severity of skin involvement.

Patients

Data were extracted from the electronic database of all patients with psoriasis treated with systemic therapies at our center. The analysis included all patients with obesity who started a systemic therapy between October 2010 and June 2018. Patients

were considered eligible for the investigation if they received at least 2 examinations (at the start of the therapy and after 3±1 months apart) over a 1-year period. For those subjects who received 1 or more systemic treatments, only the last was considered. The following data were extracted corresponding to each time point when patients received a clinical examination (3±1 months): PASI, weight, BMI, Dermatology Life Quality Index (DLQI; range 0-30) (12), and visual analogic scale for measuring itch intensity (VAS itch; score 0-100).

Assessments

The primary efficacy endpoint was to evaluate the proportion of subjects who achieved an improvement of at least 75% from baseline in the PASI score (PASI 75) at any time during the 1-year period after starting a systemic therapy.

Secondary endpoints included: a) PASI 90 and PASI 100 responses (achievement of at least 90% or 100% improvement, respectively) at any time during the 1 year treatment; b) time in weeks to attain PASI 75, PASI 90, or PASI 100 after starting therapy; c) variations of BMI, DLQI, and VAS itch during treatment.

Statistical analyses

Statistical analyses were performed using GraphPad Software, La Jolla California USA, www.graphpad.com and MedCalc Statistical Software version 19.0.7 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2019).

Categorical data are presented as absolute numbers and percentages, and continuous data as
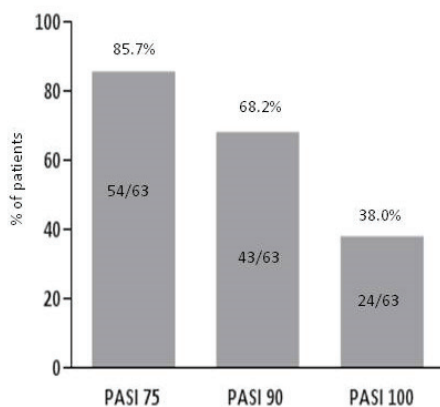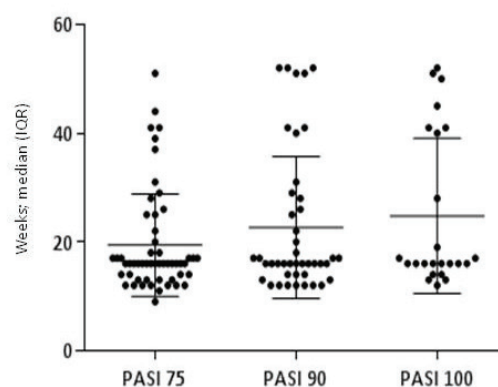
Fig. 1a

Fig. 1b

Figure 1. (a) Proportion of patients who achieved a 75%, 90%, and 100% improvement in the Psoriasis Area Severity Index (PASI 75, PASI 90, and PASI 100). (b) Median times and interquartile ranges (IQRs) in weeks to achieve PSI 75, PASI 90, and PASI 100.

medians and interquartile ranges (IQR). Wilcoxon and Fisher's tests were used as necessary.

The correlation between two continuous variables was assessed through the Spearman's rho correlation coefficient. Logistic regression analysis with the presentation of odds ratios (OR) was applied to investigate the effect of different variables on dichotomous outcomes.

Receiver operating characteristic (ROC) curve analysis was performed to identify possible optimal cut-offs, capable of splitting patients into groups with different outcome probabilities.

Those patients who failed to achieve PASI 75 during the 1-year systemic therapy, either due to treatment ineffectiveness, the occurrence of adverse events, or absence for follow-up, were censored.

RESULTS

The demographic and clinical characteristics of patients (n° 63) are shown in Table 1. All subjects were classified as obese based on a BMI ≥30 (median = 33.9; IQR=6.7). Twenty-two (34.9%) were affected by psoriatic arthritis (PsA). Comorbidities different to PsA were present in two-thirds of the subjects. At the time of study commencement, 17 (27 %) patients were receiving conventional disease-modifying drugs (cDMARDs) and the remaining 73% were receiving biologic drugs (Table 1).

Nearly half of the patients were previously treated with one or more systemic therapies (Table 1).

As shown in Figure 1, a, PASI 75, PASI 90, and PASI 100 were attained by 85.7%, 68.2%, and 38.0% patients, respectively. The median time to reach PASI 75, PASI 90, and PASI 100 was 16 weeks for all the listed outcomes with different IQRs: 6.75, 14.00, and 24.75, respectively (Figure 1, b). Of the 46 patients treated with biologics, PASI 75, PASI 90, and PASI 100 was attained by 44 (95.6%), 36 (78.2%), and 21 (45.6 %) patients, respectively. Of the 17 subjects who were administered cDMARDs, PASI 75, PASI 90, and PASI 100 was attained by 11 (64.7 %), 7 (41.1 %), and 3 (17.6 %) patients, respectively. The proportion of patients reaching PASI 75 and PASI 90 was significantly superior in those treated with biologics compared with those receiving cDMARDs (P=0.003 and P=0.01, respectively). No differences were shown between the two groups of patients in achieving PASI 100 (P=0.07).

To verify whether the improvement in psoriasis was influenced by variations in BMI, this parameter was calculated at each time point in which the subjects attained PASI 75, PASI 90, and PASI 100. At the time when the 54 patients achieved PASI 75, the median BMI was slightly but significantly higher when

Table 1. Demographic, clinical, and treatment-related characteristics of patients at baseline (n= 63)

Sex F/M	22/41
Age (years)	53 (14.8)
Duration of PsO (years), median [IQR]	14 (23.8)
PsA, n (%)	22 (34.9)
Duration of PsA (years), median [IQR]	5 (6.0)
Weight, median [IQR]	100 (22.8)
BMI (Kg/m^2), median [IQR]	33.9 (6.7)
Smokers, n (%)	26 (41.2)
Family history of PsO, n (%)	18 (28.5)
Nail involvement, n (%)	44 (69.8)
PASI, median [IQR]	12.8 (9.5)
DLQI, median [IQR]	10 (13.8)
VAS itch, median [IQR]	50 (66.7)
Patients with comorbidities, n (%)	**48 (76.2)**
hypertension	29 (60.4)
+dyslipidemia	14 (29.1)
thyropathy	12 (25.0)
diabetes type 2	10 (20.8)
mental disorders	8 (16.6)
ischemic heart disease	3 (6.2)
non-alcoholic steatohepatitis	2 (4.1)
kidney failure	2 (4.1)
non small cell lung carcinoma	1 (2.0)
§Therapies administered throughout the study, n (%)	
methotrexate	13 (20.6)
cyclosporine	3 (4.7)
acitretin	1 (1.6)
ustekinumab	28 (44.4)
adalimumab	6 (9.5)
etanercept	5 (7.9)
golimumab	1 (1.6)
secukinumab	4 (6.3)
ixekizumab	2 (3.1)
Previous systemic therapies n (%)	**45 (71.4)**
acitretin	11 (24.4)
cyclosporine	25 (55.5)
methotrexate	20 (44.4)
etanercept	13 (28.8)
adalimumab	9 (20)
infliximab	6 (13.3)
ustekinumab	2 (4.4)
golimumab	1 (2.2)
efalizumab	1 (2.2)

PsO: psoriasis; PsA: psoriatic arthritis; BMI: body mass index; PASI: Psoriasis Area Severity Index; DLQI: Dermatology Life Quality Index; VAS: Visual Analogue Scale. +Triglycerides ≥150 mg/dL and/orHDL cholesterol< 40 mg/dL. §Doses of drugs administered in the present study: i) methotrexate, 7.5-15 mg/weekly; ii) cyclosporine 2.5-5.0 mg/kg/day; iii) acitretin, 10-20 mg/day; iv) ustekinumab 45 mg subcutaneously (body weight ≤100 kg) or 90 mg (body weight >100 kg) given as one injection at the start of treatment, followed by one administration after 4 weeks and then one administration every 12 weeks; v) adalimumab 80 mg subcutaneously followed by 40 mg after 1 week and then 40 mg every 2 weeks; vi) etanercept 50 mg subcutaneously twice weekly for 12 weeks, followed by 50 mg weekly; vii) golimumab: 50 mg subcutaneously once a month; viii) secukinumab 300 mg subcutaneously at weeks 0, 1, 2, 3, and 4 followed by 300 mg once a month; ix) ixekizumab, 160 mg subcutaneously at week 0, followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12, then 80 mg every 4 weeks. Data are shown as median and interquartile range [IQR] or absolute number and percent (%).

Table 2. Odds ratios (ORs) of PASI 75, PASI 90, and PASI 100 after starting systemic therapies assessed by multivariate logistic regression analysis

Baseline variables	PASI 75			PASI 90			PASI 100		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Sex (men vs. women)	1.21	0.08-18.3	0.8	0-90	0.1-7.0	0.9	0.84	0.1-4.0	0.8
Age	0.90	0.77-1.06	0.2	0.94	0.8-1.0	0.3	0.96	0.9-1.0	0.2
BMI	0.78	0.60-1.0	0.06	0.81	0.6-0.9	0.03	0.91	0.7-1.0	0.2
Familiarity (yes/no)	4.03	0.12-127	0.4	0.54	0.08-3.2	0.5	0.22	0.04-1.1	0.07
Smoke (yes/no)	0.14	0.008-2.6	0.2	2.45	0.3-18.9	0.4	0.65	0.1-2.5	0.5
PsA (yes/no)	0.22	0.02-3.4	0.3	0.05	0.0053-0.6	0.02	0.40	0.09-1.7	0.2
Comorbidities (yes/no)	0.70	0.02-25.8	0.8	2.35	0.2-20.3	0.4	0.90	0.1-5.5	0.9
Previous systemic therapies (yes/no)	0.13	0.007-2.5	0.2	3.33	0.3-33.0	0.3	0.42	0.04-3.8	0.4
Nail involvement (yes/no)	6.0	0.2-161.6	0.2	0.95	0.09-10.0	0.9	1.07	0.2-4.8	0.9
Biologic drugs administered at T0 (yes/no)	67.0	2.7-202.18	0.01	19.28	1.7-219.2	0.01	22.64	1.6-307.2	0.01
Duration of psoriasis (years)	0.96	0.8-1.0	0.4	0.93	0.8-1.0	0.1	0.94	0.9-1.0	0.2
PASI	1.18	0.9-1.4	0.5	1.09	0.9-1.2	0.2	0.96	0.8-1.0	0.5
DLQI	1.0	0.9-1.2	0.5	1.19	1.03-1.3	0.01	1.11	0.1-1.2	0.05
VAS itch	0.9	0.9-1.3	0.8	1.0	0.9-1.0	0.8	0.98	0.9-1.0	0.2

BMI: body mass index; PsA: psoriatic arthritis; PASI: Psoriasis Area Severity Index; DLQI: Dermatology Life Quality Index; VAS: Visual Analogue Scale

compared to baseline (*P*=0.02). No significant differences in BMI variations were recorded at the attainment of either PASI 90 or PASI 100. A significant decrease in DLQI and VAS itch scores (*P*<0.0001 for both parameters) was observed in patients reaching PASI 75, PASI 90, and PASI 100, respectively.

At baseline, no correlations were found between PASI and patient BMI, age, psoriasis duration, and DLQI (data not shown). A correlation between PASI and VAS itch was recorded (*P*=0.02) but this was considered negligible due to rho=0.2.

Nine subjects failed to reach the primary endpoint (5 men, 4 women; median age 55 years, IQR 9.5; BMI 32.3, IQR 6.0; median PsO duration 16 years, IQR 26.5). Of the above 9 patients, 3 received biologic drugs (ustekinumab, adalimumab, and golimumab, respectively) and the remaining 6 received cDMARDs (1 acitretin; 5 methotrexate). Of the above 9 patients, 7 failed to attend the follow-up, 1 experienced methotrexate hepatotoxicity, and 1 experienced secondary failure of adalimumab therapy.

The results of multivariate logistic regression to explore the associations of different variables at baselines with the achievement of PASI 75, PASI 90, and PASI 100 responses are shown in Table 2. In particular, therapy with biologic drugs was positively associated with the chance of obtaining PASI 75, PASI 90, and PASI 100. The wide ranges of confidence intervals observed are due to the small sample of patients included in this study. With regard to PASI 90, BMI >31.77 (ROC curve analysis) and the presence of

PsA were negatively associated with the achievement of the above outcome. DLQI>6 (ROC curve analysis) showed a positive association with the achievement of PASI 90. At baseline, from among the 63 patients in this study, a BMI >31.7 and a DLQI >6 was recorded in 48 and 39 subjects, respectively.

DISCUSSION

This retrospective study showed that in a median time of 16 weeks the majority of patients with obesity and psoriasis treated with a systemic therapy achieved an improvement of 75% in the PASI score (PASI 75) compared with the PASI baseline (Figure 1). At the same median time, more than half the patients reached PASI 90 and one-third achieved PASI 100. Due to the greater effectiveness of biologic drugs compared with cDMARDs (13), a significant proportion of patients treated with the former class of medicines reached PASI 75 and PASI 90 (see results section). With regard to the attainment of PASI 100, the lack of significant differences between subjects who received biologic drugs compared with those treated with cDMARDs is probably due to the small sample size of patients included in this analysis.

Overall, the treatment of patients with biologic drugs was predictive of a greater probability to achieve PASI 75, PASI 90, and PASI 100 when compared to those treated with cDMARDs (Table 2).

Higher BMI values (>31.77) and the presence of PsA were negative predictors of improvement for PASI 90 but not for PASI 75 and PASI 100. In contrast,

DLQI>6 was associated with a greater probability of achieving PASI 90.

The clinical improvement seen in our patients could not be attributed to a reduction in BMI throughout the period of observation. In fact, the median value of the that parameter was greater than baseline at the achievement of PASI 75 and did not significantly change in those subjects obtaining PASI 90 and PASI 100 (see results section).

As expected, a significant reduction in both DLQI and VAS itch was observed at achievement of clinical improvement.

Data on the effectiveness of systemic therapies in patients with obesity and psoriasis are currently rather scarce and mainly designed to evaluate the effects of weight loss and BMI reduction in response to different therapies (7,9,14). The majority of available data indicate a better response in patients who experienced a reduction in BMI (9,14-16).

CONCLUSIONS

Our study had several limitations, including its retrospective nature, the reduced size of the sample, no evaluation of waist circumference, and the absence of a sample of normal-weight patients with psoriasis for comparison. Nevertheless, our real-life data indicate that PASI 75 was attained in more than two-thirds of the patients with obesity who received a systemic therapy (Figure 1, a), without a reduction in their BMI (Table 2). It is worth noting that almost 70% of patients reached PASI 90.

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