Disease Activity in Psoriatic Arthritis Index and Psoriatic Arthritis Impact of Disease Questionnaire: correlation and sensitivity to change in a real clinical setting

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Abstract

Objective

The performance of many outcome measures for psoriatic arthritis (PsA) is almost unknown in real clinical practice. Our objective was to study the correlation and sensitivity to change of the Disease Activity in Psoriatic Arthritis (DAPSA) index and the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire in a real practice setting.

Methods

This was a prospective, open, non-controlled study that included 60 consecutive patients with PsA treated with ustekinumab. Most had been previously treated with one or more biologic therapeutic agents. The correlation (Spearman's rho coefficient) and the sensitivity to change [Standardized Mean Response (SMR)] of DAPSA and PsAID were studied. Effect size values of 0.20, 0.50 and 0.80 corresponded to low, moderate and high sensitivity to change, respectively.

Results

More than 70% of patients achieved therapeutic goals (21.7% were in remission and 50% in low disease activity according to DAPSA categories). Two out of three patients reached an acceptable symptomatic state (PsAID <4). The correlation between final values of both instruments was substantial (Spearman's rho: 0.62, p<0.0001). The SMRfor the PsAID was 1.08 (0.95–1.21) and for DAPSA was 1.5 (1.37–1.63), both values corresponding to instruments with a high sensitivity to change (>0.80). The best PsAID cut-off value for identifying DAPSA remission was 3.32 with an area under the ROC curve of 0.82.

Conclusion

DAPSA and PsAID seem to be useful instruments for a more comprehensive assessment of PsA in daily practice. Our results can help to disseminate the use of these instruments in the clinical practice of many rheumatologists.

Key words

psoriatic arthritis, disease activity, impact of disease, patient-reported outcome measures, ustekinumab

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Introduction

Psoriasis and psoriatic arthritis (PsA) are immune-based diseases with a relatively high prevalence in the general population. It is estimated that approximately one third of patients with cutaneous psoriasis end up developing PsA. Psoriatic arthritis is a disease with a high degree of clinical pleomorphism, being common that the different clinical patterns of the disease change and overlap each other over time (1).

In recent years there has been a huge development in the measurements used to interpret the inflammatory activity of the disease, as well as in those instruments devoted to evaluate the response to the different modalities of pharmacological treatment (2). Despite this, there is no general consensus on which of these measures are the most appropriate for use in clinical practice. In general, most randomised clinical trials carried out in PsA evaluate its primary endpoint with instruments such as the ACR response, which is hardly used in the routine evaluation of these patients. On the other hand, some relevant PsA outcome measures recommended by EULAR, such as the *Minimal Disease Activity* (MDA) response, the *Disease Activity in PSoriatic Arthritis* (DAPSA) score categories, or the *Psoriatic Arthritis Impact of Disease* (PsAID) questionnaire, do not seem to have a widespread use in daily clinical practice (3, 4).

One of the reasons for this unequal penetration of these tools in clinical practice may lie in the greater or lesser degree of complexity in terms of its interpretation and feasibility in day-to-day consultation, but another compelling reason is that the clinimetric properties of some of these measures are barely known in the real clinical practice scenario.

Disease management in PsA is a complex and, in most cases, incomplete task. This is because in daily practice, most rheumatologists base their clinical and treatment decisions on measures that are usually obtained from the physical examination of the patient, such as the swollen and painful joint counts, without taking into account other patient-derived data (5, 6). Most of the time, the information obtained from patient-reported outcome measures (PROM) is hardly taken into account, so that, only in few instances, the measures reported by clinicians are adequately balanced with those reported by patients in the clinical and therapeutic decision making (5, 6).

For all the above, it is of paramount importance to clinically test the disease activity tools (clinician's viewpoint) together with those measurements that assess the impact that the disease generates on patients' lives (patient's viewpoint). In this way, we could have a more comprehensive view of what really happens in the day to day of patients with PsA. Moreover, it is essential to carry out this clinimetric exercise in the real clinical practice scenario.

Following the above considerations, we aimed to evaluate the correlation between, and the sensitivity to change of, two of the instruments whose use is currently booming in PsA, such as DAPSA and PsAID (7). The results of this study can help disseminate the use of both tools in the daily management of these patients.

Patients and methods

In this open non-controlled prospective observational study, 60 patients diagnosed with PsA according to CASPAR criteria (8) were consecutively included. Only patients with active disease, treated with ustekinumab according to the PsA management recommendations of the Spanish Rheumatology Society, were included (9). For this study, both bionaïve and patients previously exposed to other biologic agents were included. Patients were studied following a specific study protocol that included analytical, clinical, and radiological variables. The study period extended from July 2017 to December 2018. Before starting treatment, patients signed an informed consent form for the use of this class of drugs. This study was carried out following the good clinical practice guidelines of the Helsinki declaration and the clinical research ethics committee of our centre approved the final version of the study (ref. HUCA EO 12/18).

Disease activity was evaluated according to the DAPSA, which is a composite index devoted to the assessment of peripheral articular involvement

in PsA. It is calculated linearly adding 5 variables: 1) number of inflamed joints on a 66 joint count, 2) number of painful joints on a 68-joint count, 3) pain visual analogue scale (VAS), 4) patient´s global disease activity VAS, and 5) C-reactive protein (CRP). A shorter version, without CRP, is called clinical DAPSA (cDAPSA). Depending on the result, disease activity can be classified into four groups: remission (0–4 points), low disease activity (5–14 points), moderate disease activity (15–28 points) and high disease activity (>28 points) (10).

For the assessment of disease impact on patients' lives, we used the PsAID questionnaire. PsAID-12 is used in clinical practice, and the abbreviated PsAID-9 is for clinical trials. In PsAID-12, the following items are included: pain, fatigue, skin problems, work and leisure, disability for daily activity, the sensation of discomfort and irritation, sleep difficulties, disease coping, anxiety and uncertainty, embarrassment, social participation and depression. Each item has its particular weighting. The global score ranges from 0 (best status) to 10 (worse status). A PsAID score below 4 is established as an acceptable symptomatic state for patients (4).

Statistical methodology

A descriptive statistical analysis of all the variables was performed, including central tendency and dispersion measures for continuous variables, and absolute and relative frequencies for categorical variables. Student's *t*-test, Mann-Whitney U-test or Kruskall Wallis H test were used to compare quantitative variables and Pearson's chi-square or Fisher's exact tests for qualitative variables. Concordance between instruments was assessed using Cohen's kappa (κ) and was considered as follows: <0.20 = poor, 0.21–0.40 = fair, 0.41–0.60 = moderate, 0.61–0.80 = good, and 0.81–1.00 = very good. Differences between final and baseline mean of DAPSA and PsAID were analysed with the McNemar p-test. Correlation between DAPSA and PsAID, both at baseline and the end of the study, was assessed by the Spearman's rho coefficient. The sensitivity to change of both instruments was measured using the standardised mean response (SMR). In general, effect size values of 0.20, 0.50 and 0.80 correspond to instruments with low, moderate and high sensitivity to change, respectively. Receiver operator curves (ROC) were also constructed to find the best cut-off point for the PsAID values that would serve to identify the remission and low disease activity categories according to the DAPSA. Finally, a Kaplan-Meier drug survival curve was constructed. Data were analysed using SPSS v. 19.0 statistical software (IBM Corp. NY, USA).

Results

The study included 37 women and 23 men, mean age 55±8.7 years. The median duration of arthritis was 4 years (IQR: 2–8.2), while the median duration of psoriasis was 13 years (IQR: 5–25). There was a high frequency of traditional cardiovascular risk factors, so that 26.7% of patients were hypertensive, 15% were diabetic, 36.7% were smokers, 50% were obese, 16.7% of patients had hyperuricaemia. Out of 60 patients, 5 (8.3%) had had an adverse cardiovascular event. As for the articular patterns, 35% presented oligoarthritis, 15% polyarthritis, while 50% presented axial forms, most of them mixed (axial + oligoarthritis or axial + polyarthritis). Regarding typical characteristics of PsA, 38.3% had distal interphalangeal joint involvement, and 25% had dactylitis. Table I summarises baseline characteristics of the study population.

Regarding the previous exposure to biological drugs, 25% had used a single anti-TNF-α agent, 33.3% had used two anti-TNF-α, 10% 3 anti-TNF-α, and 1.7% had used 4 or more of these agents. 30% were bio-naïve. Half of the patients were using methotrexate concomitantly with ustekinumab. In most cases (75%) withdrawal of anti-TNF-α was due to lack or loss of efficacy. Median duration of ustekinumab therapy was 6 months (IQR: 3–10). Patients in remission had used the drug on average for 10.16±8.45 months, compared to 6.7±4.2 months for those who were not in remission ($p<0.05$).

The average baseline DAPSA was 20.4±5.6, while the final DAPSA was 10.8±5.8. The average difference between the final and baseline value was 9.53±5.52, 95% CI: 7.54–11.52, McNemar $p<0.0005$. In baseline situation, 11.7% of the patients had low disease activity, 68.3% corresponded to moderate DAPSA activity, and 20% were in the high activity category. At the closing visit, 21.7% of patients were in DAPSA remission, 50% in low disease activity, 26.6% were in the moderate category, and only one was in DAPSA high activity (1.7%). That is, more than 70% of patients achieved therapeutic goals (remission and low disease activity).

The Spearman's rho correlation between baseline values of DAPSA and PsAID was 0.34 ($p=0.021$), while the correlation between final values of both instruments was substantial (rho: 0.62,

Table I. Baseline characteristics of the study population.

Number of patients	60
Age (years): mean ± SD	55 ± 8.7
Gender distribution: n (%)	
Men	23 (38.3)
Women	37 (61.7)
Disease duration (years): median (IQR)	
Psoriasis	13 (5-25)
Arthritis	4 (2-8.2)
Family history: n (%)	
Psoriasis	24 (40)
PsA	7 (11.7)
Comorbidities: n (%)	
Hypertension	16 (26.7)
Diabetes	9 (15)
Smokers	22 (36.7)
Obesity	30 (50)
Hyperuricaemia	10 (16.7)
CVD events	5 (8.3)
Articular patterns: n (%)	
Oligoarthritis	21 (35)
Polyarthritis	9 (15)
Axial plus peripheral	30 (50)
Typical disease features: n (%)	
Dactylitis	15 (25)
Enthesitis	15 (25)
DIP disease	23 (38.3)
Erosive disease	15 (25)
Previous exposure to biologics: n (%)	
Bio-naïve	18 (30)
1 anti-TNF-α	15 (25)
2 anti-TNF-α	20 (33.3)
3 anti-TNF-α	6 (10)
≥4 anti-TNF-α	1 (1.7)
MTX use: n (%)	30 (50)
DAPSA categories: n (%)	
LDA	7 (11.7)
MDA	41 (68.3)
HDA	12 (20)
PsAID: mean ± SD	7.3 ± 3.5

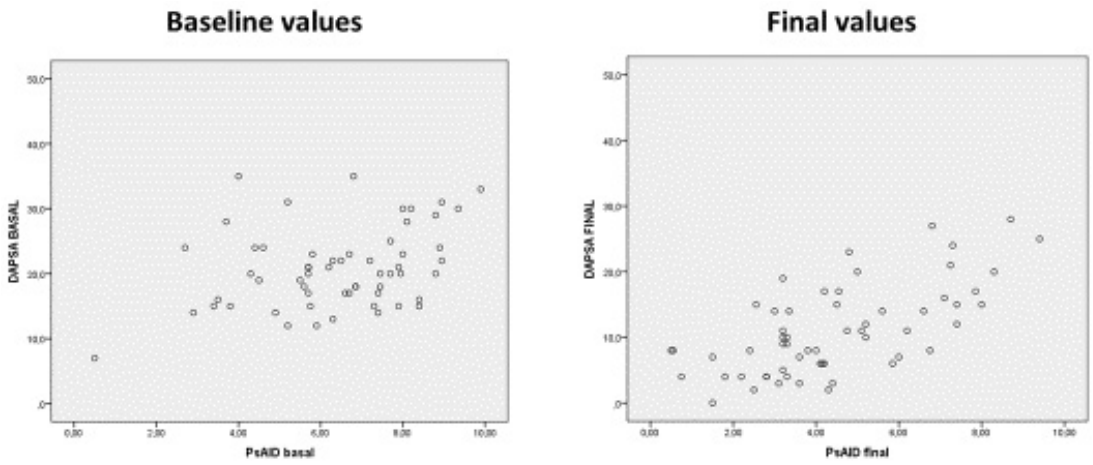

Fig. 1. Graphs of basal and final correlations between the DAPSA and the PsAID. Spearman's rho coefficient was modest in the baseline situation (rho: 0.34), however, the final correlation was substantial (rho: 0.62).

$p<0.0001$), Figure 1. However, κ concordance values between DAPSA remission (κ: 0.34) and DAPSA low disease activity (κ: 0.37) with a PsAID <4, were only fair.

Of the 60 patients, 66.7% achieved a PsAID <4 (acceptable symptomatic state). Baseline PsAID was 7.3±3.5 and the final score was 3.8±4.2. The SMR for the PsAID was 1.08 (0.95–1.21), with the effect size of that change, using the standard deviation of the means, of 0.90 (high sensitivity to change). On the other hand, the SMR corresponding to the change of the DAPSA was 1.5 (1.37–1.63), which again corresponds to a high sensitivity to change (>0.80).

The survival of the drug according to the Kaplan-Meier curve was 81.3% during the first year.

Finally, the best PsAID cut-off value for identifying DAPSA remission was 3.32 with an area under the ROC curve of 0.82.

Six patients stopped Ustekinumab, four because of lack or loss of efficacy and two due to poor tolerance. No cases of tuberculosis, opportunistic infections or incidental neoplasms were detected during follow-up. There were no hospital admissions related to the drug.

Discussion

This study included a population of patients with active PsA. Most of them had experienced therapeutic failures with one or more anti-TNF-α agents. After ustekinumab treatment, we verified that the PsAID is a valid instrument to evaluate the impact of PsA on different facets of the patient's life. Although baseline rho and κ-values between DAPSA and PsAID were modest, at the end of the study, Spearman´s rho correlation between both was substantial (rho >0.60). In addition, the sensitivity to change yielded high SMR values, which indicates the validity of this instrument to measure the changes in several aspects of the quality of life of the patient after the use of a therapeutic intervention. On the other hand, we have also verified that the DAPSA is a useful instrument to evaluate disease activity in clinical practice settings, since the sensitivity to change was also higher than 0.80. In summary, both instruments showed high SMR values after the use of ustekinumab, which provides robustness to both tools with respect to their use in daily practice to assess therapeutic success.

There have been some doubts about the role of ustekinumab in the treatment of patients with PsA in real life (11). However, our data show that this drug is effective and safe, both in patients who have been previously exposed to other biologics but also in bio-naïve patients

In recent years, we have witnessed an intense search for instruments that could reliably capture what happens to PsA patients, both from the point of view of objective measures of disease activity, but also from a more subjective point of view, related to the experiences and perceptions lived by patients with this disease (12). Although there are no clear consensus measures in these aspects, in the last few years certain tools, such as DAPSA and PsAID, have gained strong support to evaluate the aforementioned aspects. Thus, for example, a recent work found a good concordance rate between DAPSA and PsAID in patients with PsA under systemic treatment (13). Our work aimed to give extra support to these measures so that they could be incorporated into the routine evaluation of these patients.

Other measures such as the MDA response have also been established as good treatment targets, since patients who achieve this stringent goal usually have PsAID values consistent with an acceptable symptomatic state as well as less structural damage (14, 15). In general, the concordance between the MDA response and the DAPSA remission or low activity values is modest (16). However, any of them is recommended in order to accomplish with the treat to target strategy in spondyloarthritis and PsA as recently proposed by EULAR (3). We have not included MDA values in our report, but as we commented before, different works support the use of DAPSA as an adequate tool to assess both disease activity and response to treatments in PsA (13, 16, 17).

Patients with PsA experience a serious impairment in their quality of life (18). This is due to the coexistence of multiple variables, most of which are not usually collected in clinical practice (18). In 2014, EULAR designed and validated a tool with the aim of evaluating the impact that PsA generates on patients' lives (4). Different facets of patients' lives were evaluated (pain, sleep, fatigue, work, leisure, mood, coping, embarrassment, etc.), and all this information was integrated into a

questionnaire of 12 items with a final score ranging from 0 to 10 (from better to worse situation). A cut-off point of 4 was also defined, below which the patient was considered to be in an acceptable symptomatic state (4). Given that PsAID is an instrument that includes many variables, not all directly related to the inflammatory activity of the disease, it is not surprising that kappa values between PsAID and DAPSA in our study were not high. In this sense, our data coincide with other studies recently reported in this regard (16).

When looking for which cut off point of PsAID identified a state of DAPSA remission, we obtained a value of 3.2, that is, a value below 4, which supports this cutoff as a treatment goal to be achieved in clinical practice.

The therapeutic results obtained with ustekinumab in this study were optimal. Yet, this study does not allow more inferences regarding the effectiveness of this agent because the small sample size is not the most appropriate for this purpose. Additionally, tolerability and safety of this drug was optimal (6 patients discontinued the drug, and of these only 2 did so because of a tolerance or safety problem).

This study has of course some limitations. Being an uncontrolled observational study, it is not adequate to extrapolate its effectiveness and safety results to other settings. The median time of ustekinumab use was not very prolonged (less than 12 months), which does not allow us making medium- or long-term inferences about its effectiveness-safety. Half of the patients included in this study had axial involvement and specific instruments for this domain (BASDAI or ASDAS) were not used, so it is difficult to ensure to what extent the DAPSA captured this disease domain. In any case, in a recent report the PsAID was able to capture part of this domain, showing a good clinimetric alignment with the BASDAI remission. On the other hand, the sensitivity to change, as well as the correlation with DAPSA, has been made by taking the instrument as a whole, without an item by item weighting (that is, we do not know which of the items of the PsAID had more weight in the sensitivity to change). In addition, it would have been interesting, for example, to analyse the behaviour of DAPSA and PSAID in relation to some additional clinical features such as presence of comorbidities, PsA phenotype, or number of previous TNFi used. Nonetheless, the small number of patients precluded any additional assessment in that regard. Finally, the behaviour of these tools refers to ustekinumab in particular. We do not know therefore its behaviour with other therapeutic interventions. However, as a whole, PsAID seems to adequately capture the changes that occur in patients' lives after a therapeutic intervention, while DAPSA is an adequate instrument to assess disease activity changes in the setting of daily practice.

Conclusions

The PsAID is a useful instrument to measure the impact of PsA on patients' lives. It behaves appropriately to capture the changes in these aspects after the use of a therapeutic agent like ustekinumab. DAPSA and PsAID seem useful instruments for a more comprehensive assessment of PsA in daily practice. Our results can help to disseminate the use of these instruments in the clinical practice of many rheumatologists.

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