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ORIGINAL ARTICLE

Treatment of Moderate-to-Severe Psoriasis in Clinical Practice: A Survey of Spanish Dermatologists

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KEYWORDS

Psoriasis;
Disease management;
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Abstract

Background and objectives: Various treatment options are available for use in moderate-to-severe psoriasis and election is dependent upon the clinical criteria applied by the attending physician. We undertook a survey among dermatologists to assess the treatment of moderate-to-severe psoriasis currently used in clinical practice in Spain.

Methods: A cross-sectional study was performed by sending a questionnaire to dermatologists in Spain who treat patients with moderate-to-severe psoriasis. The questionnaire comprised 33 items distributed in 6 sections: profile of the dermatologist, case load, patient profile, follow-up and management of the disease, treatment regimens, and assessment of pharmacological treatments.

Results: According to the responses of the 164 dermatologists surveyed, 6.8% of patients seen in their clinics have moderate-to-severe psoriasis; of those, 45.8% receive systemic treatment and 22.9% are treated with biologic drugs. In many of those patients (50.2%), the dermatologist felt that a change in treatment was necessary; in 51.1% of cases, this change would be from systemic therapy to a biologic drug. The principal reason for the change (50.8%) would be lack of efficacy or the appearance of adverse effects. Efficacy and safety were considered essential criteria in the choice of an appropriate treatment (82.9% and 28.0% of dermatologists, respectively). Patient quality of life was also considered an essential consideration in choice of treatment by 28.0% of dermatologists.

Conclusions: Optimal treatment for moderate-to-severe psoriasis should be effective and safe, and improve patient quality of life. This makes it essential to use drugs with an excellent efficacy and safety profile.

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PALABRAS CLAVE

Psoriasis;
Manejo de la
enfermedad;
Encuesta de opinión;
Dermatología;
España

Realidad terapéutica de la psoriasis moderada-grave en España. Encuesta de opinión**Resumen**

Introducción y objetivos: Las estrategias terapéuticas existentes para la psoriasis moderada-grave son múltiples, siendo el criterio clínico fundamental para su elección. Para conocer la realidad terapéutica de la psoriasis moderada-grave, se realizó una encuesta de opinión basada en práctica clínica habitual en España.

Método: Estudio transversal mediante encuesta a dermatólogos que tratan a pacientes con psoriasis moderada-grave en España. La encuesta constaba de 33 ítems distribuidos en 6 secciones: perfil del dermatólogo, carga asistencial, perfil de paciente, seguimiento y manejo terapéutico de la enfermedad, pautas de tratamiento y valoración de fármacos.

Resultados: Según los datos de opinión y experiencia de los 164 dermatólogos encuestados, el 6,8% de los pacientes atendidos en consulta presentarían psoriasis moderada-grave, de los que el 45,8% estarían tratados con un fármaco sistémico y el 22,9% con uno biológico. En muchos de estos pacientes (50,2%) se haría un cambio de tratamiento, de sistémico a biológico en el 51,1% de los casos. El principal motivo de cambio (50,8%) sería una falta de eficacia o aparición de efectos adversos. La eficacia y seguridad serían criterios imprescindibles a considerar para la elección de un tratamiento óptimo (82,9 y 28,0% de los dermatólogos, respectivamente). Un 28,0% de los dermatólogos consideró también imprescindible la valoración de la calidad de vida de los pacientes para instaurar un tratamiento.

Conclusiones: El tratamiento óptimo para la psoriasis moderada-grave debería ser eficaz, seguro y capaz de mejorar la calidad de vida del paciente. Para ello, es imprescindible el uso de fármacos de elevada eficacia y seguridad.

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Introduction

Psoriasis is a chronic inflammatory skin disease marked by periodic flare-ups. Worldwide, millions of patients are affected. In Spain the prevalence is around 2% and the incidence around 1.4%, but a rising trend has been reported.^{1,2} While rarely life-threatening, psoriasis causes significant loss of health-related quality of life (HRQOL), especially in physical, emotional, sexual, work-related, and economic domains.³

In routine clinical practice in dermatology, the severity of psoriasis is usually assessed by estimating the percentage of body surface area (BSA) affected and the Psoriasis Area and Severity Index (PASI).^{4,5} Overall, psoriasis patients account for 8.7% of dermatology consultations in Spain,⁶ and between 20% and 30% have moderate to severe forms of the disease.³

The wide-ranging treatments currently available mainly aim to achieve adequate clinical control and individual tailoring of therapy is advised.^{3,7,8} Moderate to severe forms are usually treated with conventional systemic or biologic drugs.³ Sources agree that the treatment of choice in such cases will be systemic,⁹⁻¹¹ even though significant adverse effects may occur.⁸ As biologic agents offer better short- and medium-term efficacy and safety profiles than traditional systemic drugs, they are recommended for adults with moderate to severe disease that has not responded to other

therapeutic measures, those for whom other measures are contraindicated or who develop intolerance, or those who have experienced adverse effects; biologics are also used when toxicity is suspected.¹² These agents therefore represent an important step forward, as they lead to significant improvement in disease parameters and in HRQOL as well, contributing to treatment adherence.¹³⁻¹⁵

Clinical practice guidelines are highly useful when establishing an approach to treating moderate to severe psoriasis, but dermatologists' experience and opinions are also key components in the actual choice of therapy. In this study we aimed to determine how dermatologists are managing moderate to severe psoriasis in routine clinical practice and to identify the criteria the dermatologists use when making choices.

Methods**Study Design**

This cross-sectional questionnaire survey sought information on Spanish dermatologists' management of moderate to severe psoriasis. Respondents were working in a variety of public and private health care settings (including hospitals, health service clinics, and private practices) throughout Spain. All respondents had to have had experience with the

routine care of patients with moderate to severe psoriasis (BSA ≥ 10 or baseline PASI score ≥ 12).

The specially designed questionnaire had 33 items in 6 sections covering information on the dermatologist, the caseload, the patients, the practitioner’s follow-up and management of the disease, treatment regimens, and opinions held about drugs used to treat the disease. Eligible dermatologists were contacted and the objectives of the study and the questionnaire design were explained, with specific mention that data would be considered confidential. All respondents gave their signed informed consent before participating. Questionnaires were completed anonymously from July through October 2008. Submission of the questionnaire to the investigator was also anonymous (in a sealed envelope) to ensure that the dermatologists would feel free to answer frankly.

Study Variables

Data collected were as follows, by section: age, sex and extent of experience (profile of the dermatologist); mean number of patients and types of patient (caseload); percentage of patients on active treatment, on combination therapies, and reasons for changing therapy (patient profile); frequency of visits, tools used in follow-up assessments, therapeutic goals, criteria for choice of treatment, and treatment availability (follow-up and management of the disease); treatments chosen, basis for selection, presence and severity of adverse effects (treatment regimens); and opinions of the various treatments used. Variables requiring the respondents’ evaluation were assessed on a scale of 1 to 5, in which 1 was unimportant and 5 essential, based on clinical criteria and practice experience.

Statistical Analysis

A sample of 200 participants was considered necessary to estimate differences between dichotomized variables with a significance level of *P* less than .05 and a level of precision of $\pm 7.5\%$. We assumed that 15% of questionnaires would be incomplete.

Descriptive statistics were compiled with the SPSS package (version 17.0 for Windows).

Results

A total of 210 questionnaires were sent; 164 were returned completed (response rate, 78.1%). Hospitals were the practice setting of 98.2% of the responding dermatologists, although 43.9% treated outpatients. Fifty percent of the respondents had a private practice, and 56.7% were men. Their mean age was 43.0 years (95% confidence interval [CI], 34.2-51.8 years) and the mean number of years practicing was 14.5 years (95% CI, 5.7-23.3 years).

In the opinion of the surveyed dermatologists, one of their principal aims when deciding on the best approach to take in treating patients with moderate to severe psoriasis would be to improve HRQOL (rated essential by 74.8%) (Figure 1). The respondents also thought a reduction in BSA should be targeted, along with avoidance of adverse effects.

According to the Spanish dermatologists’ estimates, they see a mean of 146.2 (95% CI, 86.6-205.8) patients per week; 13.9% of the visits are related to psoriasis and 6.8% of the cases are moderate to severe. Psoriasis patients are seen quarterly by 59.5% of the surveyed specialists and

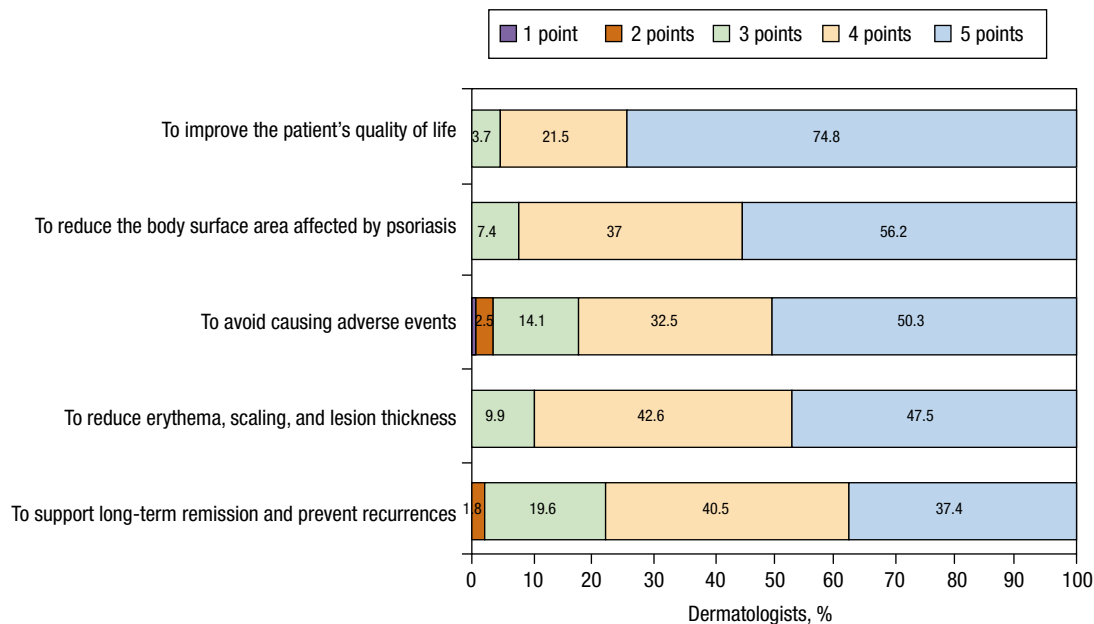


Figure 1 Therapeutic aims the dermatologists considered when deciding on a treatment for moderate to severe psoriasis. Responses were rated on a scale of 1 (unimportant) to 5 (essential).

more frequently (monthly or every 2 months) by 36.8%. During follow-up, PASI scores and BSA were reportedly used by 84.0% and 36.2%, respectively, and 17.8% of the respondents declared they used HRQOL instruments such as the Dermatology Life Quality Index. All reported recording clinical and biochemical findings routinely on follow-up visits.

Approximately 45.8% of patients with moderate to severe psoriasis seen by these dermatologists were reported to be taking a systemic drug and 22.9% were taking a biologic agent, and most (70.7%) were between the ages of 31 and 65 years. The percentage of patients not on a systemic or biologic agent was estimated at 31.3%, in accordance with usual practice. The dermatologists with fewer than 10 years' experience reported that 76.1% of their patients were taking systemic or biologic drugs, whereas those with 10 to 20 years' experience estimated that 63.5% of theirs were so-treated. For the most experienced (>20 years), the mean estimated percentage was 63.8%

The respondents reported that 50.2% of patients with moderate to severe psoriasis taking conventional systemic drugs or biologic agents required a change; in 51.1% of the cases, a conventional drug would be withdrawn and a biologic used in its place. The reason for switching therapy in 50.8% of the cases was lack of efficacy; the second-leading reason was the possible appearance of adverse effects (Figure 2).

The dermatologists expressed the opinion that first-line treatment options for moderate psoriasis, in order of preference, would be methotrexate, acitretin and psoralen plus UV-A (PUVA) (Table). For severe psoriasis, the

preferences would be ciclosporin A and 3 biologic agents—etanercept (43.6%), infliximab (37.4%), and adalimumab (30.7%). In the experience of these specialists, the 3 criteria considered essential when choosing a first-line treatment were efficacy (82.9%), adverse effects (28.0%), and the patient's HRQOL (28.0%).

More than 80% declared that most psoriasis treatments were available to them, with the exception of hydroxyurea

Table 1 Drugs the Responding Dermatologists Considered Their First Choices for Moderate to Severe Psoriasis

	Moderate Disease	Severe Disease
Methotrexate, n (%)	87 (53.4%)	46 (28.2%)
Ciclosporin A, n (%)	56 (34.4%)	89 (54.6%)
Acitretin, n (%)	69 (42.3%)	21 (12.9%)
Hydroxyurea, n (%)	17 (10.5%)	6 (3.7%)
Corticosteroids, n (%)	30 (18.4%)	8 (4.9%)
Etanercept, n (%)	33 (20.2%)	71 (43.6%)
Efalizumab, n (%)	28 (17.2%)	39 (23.9%)
Infliximab, n (%)	11 (6.7%)	61 (37.4%)
Adalimumab, n (%)	21 (12.9%)	50 (30.7%)
PUVA, n (%)	69 (42.3%)	18 (11.0%)
NB-UV-B, n (%)	62 (38.0%)	15 (9.2%)

Abbreviations: NB-UV-B, Narrow-band UV-B irradiation; PUVA, psoralen plus UV-A irradiation.

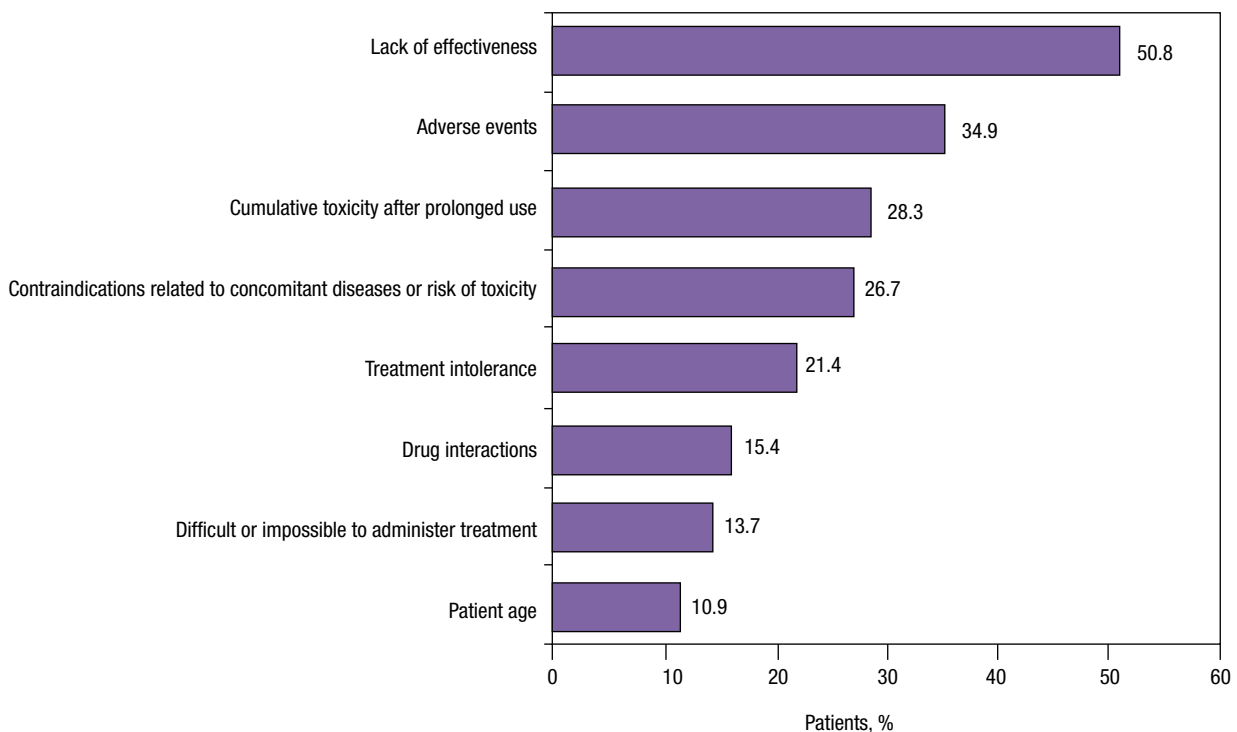


Figure 2 Reasons for switching patients from systemic to biologic drugs.

(which was not among the options 22.0% could prescribe), PUVA (51.0% had no access), and narrow-band-UV-B (NB-UV-B) (unavailable to 71.0%). The main reasons for limits placed on the availability of certain treatments were budget constraints within a health care center, the need

for internal authorization for use of some medications, or internal prescribing protocols.

Once a conventional systemic or biologic treatment was prescribed, 73.2% reported being particularly watchful for signs of kidney or liver failure (Figure 3). Furthermore,

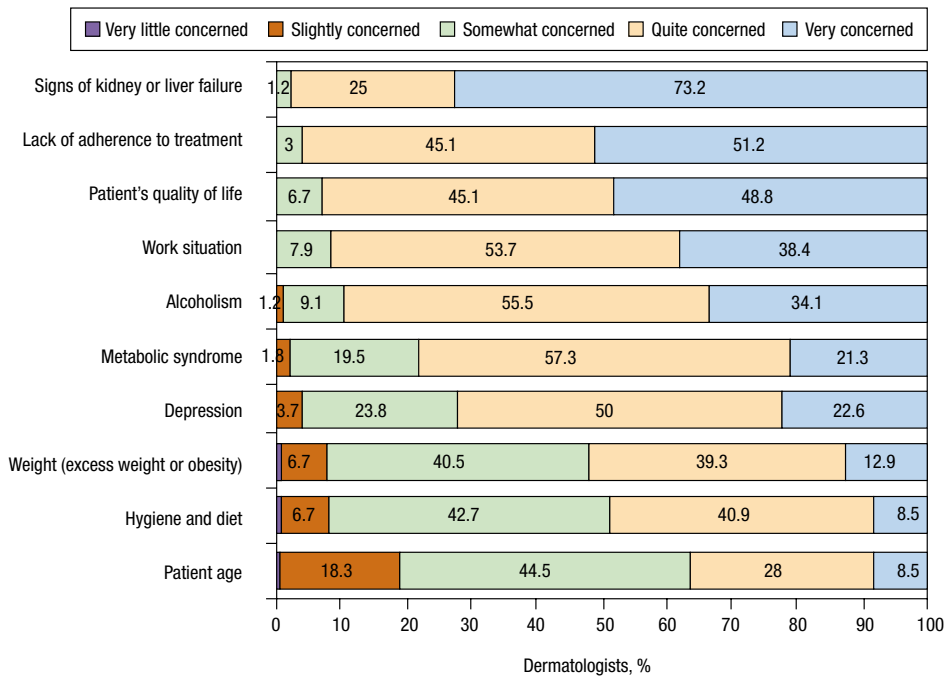


Figure 3 The dermatologists' patient-specific concerns when prescribing a systemic or biologic drug.

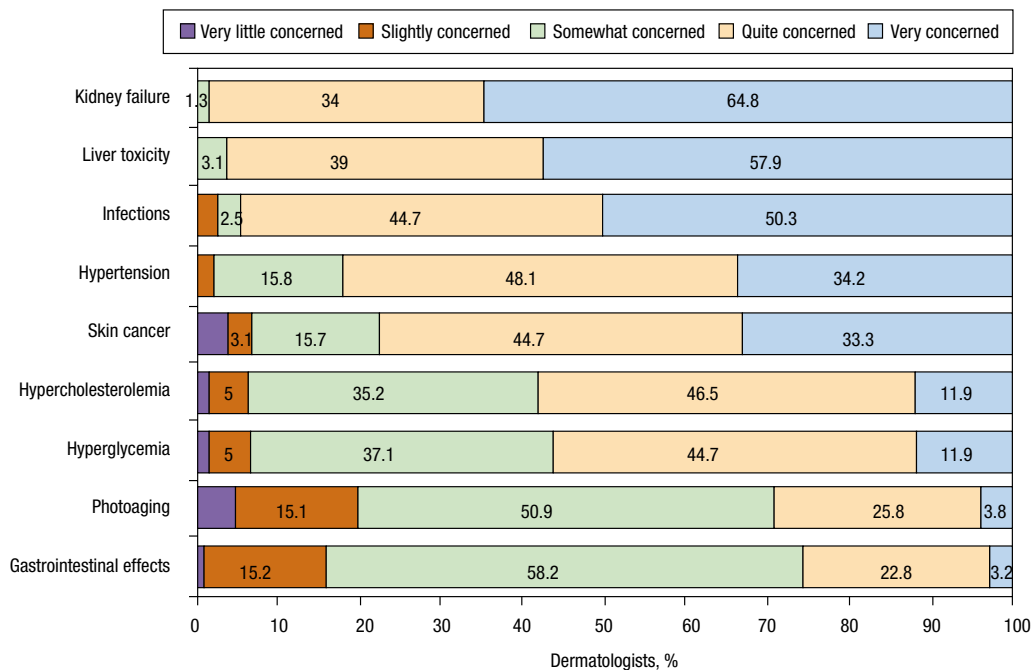


Figure 4 The adverse effects the dermatologists are concerned about when prescribing a conventional systemic or biologic drug.

51.2% were concerned about adherence to the prescribed treatment, and 48.8% had concerns for their patients' HRQOL. Kidney or liver failure and infections were the adverse effects the dermatologists named as their main concerns (Figure 4).

The likelihood of adverse effects was highest (high or very high) for patients treated with hydroxyurea or corticosteroids according to the survey (51.3% and 48.9%, respectively) (Figure 5). In contrast, these dermatologists thought that the likelihood of adverse effects would be low or very low with phototherapy (NB-UB-B, 77.9%; PUVA, 65.1%) and biologic agents, particularly etanercept (77.3%) and adalimumab (66.0%).

The attributes considered essential for an optimum treatment for moderate to severe psoriasis were efficacy (4.9 [95% CI, 4.5-5.3] points on the scale) and safety (4.7 [95% CI, 4.2-5.2] points). Both attributes were better for biologic agents than for conventional systemic drugs according to 70.6% and 59.6% of the respondents, respectively.

Discussion

This survey of Spanish dermatologists' opinions has identified the main criteria they use routinely when deciding on the most appropriate treatment regimens for patients with moderate to severe psoriasis and when monitoring treatment response. Approximately 14% of patients in dermatology practices come for treatment of psoriasis and about 6.8% of the cases are moderate to severe. These percentages are clearly higher than those published in 2000,⁶ and there may be a rising trend.

However, the increases may also be attributable to the fact that the dermatologists who participated are experienced in treating this type of patient and may therefore have larger psoriasis caseloads than the average dermatologist would. The fact that the data come from the surveyed dermatologists' own experience-based estimates may also tend to favor overestimation of the number of psoriasis patients they treat.

The dermatologists' estimates of their prescription of systemic and biologic treatments for patients with moderate to severe psoriasis are interesting because the percentages of patients on conventional systemic drugs (45.8%) or biologics (22.9%) are higher than those reported previously.^{16,17} The routine use of these drugs to treat patients who until now have been considered undertreated^{16,17} may be increasing. However, 31.3% of patients with moderate to severe psoriasis have continued to receive no conventional systemic or biologic treatment, although change may be occurring as a result of the application of clinical practice guidelines³; in fact, we saw that the percentage of such patients was lower (23.9%) in the practices of dermatologists with fewer than 10 years' experience.

Most of the dermatologists reported recording the PASI score to monitor severity during follow-up, and this index is indeed the one usually used for that purpose.¹⁸ Only 17.8% of our respondents reported using HRQOL questionnaires routinely, however, in spite of the recognized negative impact of this disease on patients.^{17,19} HRQOL assessment had previously been reported to be on the rise,²⁰ indicating greater commitment to a more holistic approach to managing psoriasis and confirming, in accordance with recent guidelines,³ that improvement of this aspect is a

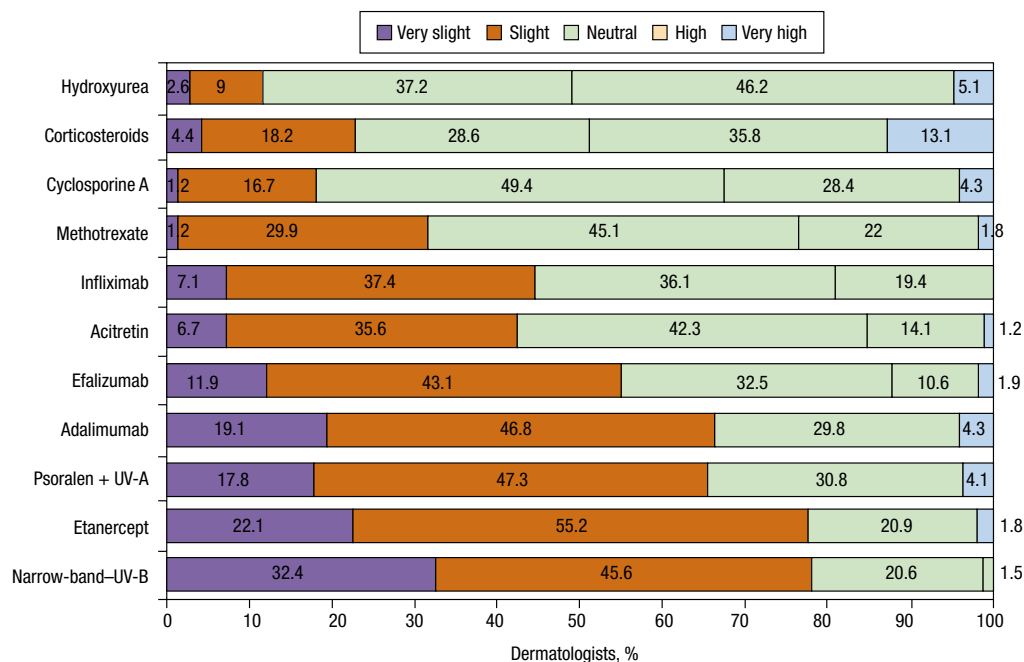


Figure 5 The dermatologists' opinions about the probability that treatments for moderate to severe psoriasis will lead to adverse effects.

fundamental therapeutic target. This is particularly the case if we consider that improvement in HRQOL will lead to greater patient perception of satisfaction with treatment and hence greater adherence.^{13,14,21} In the present study, however, we did not explore this point exhaustively. The literature provides evidence that physicians are not alone in their concerns for improving care: patients are increasingly involved with the management of their disease, seeking information about their treatments and asking for changes.¹⁶

Efficacy and safety are the main criteria to consider when deciding on a first-line treatment in the opinion of the dermatologists who responded to this survey. Nonetheless, many of the treatments considered for moderate to severe psoriasis (methotrexate, acitretin, ciclosporin A) have been shown to have significant adverse effects on the kidney, the liver, or the developing fetus.⁸ These treatments, therefore, would require careful follow-up, particularly in view of the dermatologists' report that infections and kidney and liver failure are the adverse events that most concern them. Another drug with serious adverse effects, hydroxyurea, is being chosen for a considerable percentage of patients (10.5% of patients with moderate psoriasis and 3.7% of those with severe disease). This finding is particularly interesting given that it contrasts with the lack of recommendations on the use of hydroxyurea in current consensus-based guidelines. Hydroxyurea has proven to be highly effective when other more commonly used treatments fail²²; however, its routine use is rare in psoriasis, suggesting that it is being prescribed in combination with other therapies in certain patients.^{3,23}

The safest treatments for moderate to severe psoriasis, according to the clinical experience of 75% of the respondents, are NB-UV-B therapy and etanercept. In the category of systemic and biologic drugs, it was clear that the respondents felt that the efficacy and safety profiles of biologics were superior to those of conventional systemic drugs, a finding that is consistent with the literature.^{14,15,24} To analyze the meaning of discrepancies between the most often used drugs and those considered optimal, the situations in individual health care centers should be taken into account, as a variety of reasons may be reflected or access to certain treatments may be subject to local constraints.

Design limitations of this study include the lack of collection of information on reasons for choices and the fact that some dermatologists declined to participate, with the result that the size of the sample was slightly smaller than foreseen. Sample size did not affect the findings greatly, however, given that the level of precision of the study was $\pm 7.6\%$ rather than the anticipated $\pm 7.5\%$. Another limitation is that the results reflect the personal opinions of the participating dermatologists, which are subjective. The assurance of anonymity, however, allowed the respondents to freely report how they practice routinely, thus providing valuable information that cannot be obtained from case reports.

Conclusion

The treatment received by the patients of these participating dermatologists is consistent with general guidelines for

management of psoriasis, although in many cases the conventional systemic drug regimens prescribed have to be changed, mainly due to therapeutic failure or adverse effects.

In the respondents' opinion, the optimal treatment for moderate to severe psoriasis should be effective and safe so that it improves the patient's HRQOL. A chosen drug must therefore offer a high degree of efficacy and few or no unwanted side effects. The dermatologists feel that biologic agents are superior to conventional systemic drugs on both counts, even though biologics are used less often in routine practice.

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Conflict of Interest

The authors declare that they have no conflicts of interest.

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