

Review Article

Psoriasis in the elderly. Do we know how to manage it?

老年人的銀屑病：我們懂得怎樣治理嗎？

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Psoriasis is a chronic, autoimmune, inflammatory disease that affects the skin and joints. It is characterised by disfiguring, sharply demarcated scaling plaques that typically affect the knees, elbows, sacrum, scalp and may be mild to severe in presentation. The incidence of this disease appears to be increasing in parallel with age. The elderly population is often characterised by multiple comorbidities and polypharmacy. Psoriasis management in these patients may be difficult for this reason and we can categorise them as high-need patients with important repercussions of the disease on their quality of life.

銀屑病是一種慢性自身免疫性炎性疾病影響皮膚和關節。它的特點是毀容性、邊界清晰的脫屑斑塊，影響膝、肘、骶骨、頭皮，病徵可以從輕微至嚴重。這種疾病的發生率似乎隨年齡增長而增加。老年人口的特點是其合併病症及多重用藥。治療牛皮癬患者可能因為這些原因變得困難，我們可以將它們列作高需求類的患者並重新考量病情對他們生活品質的影響力。

Keywords: Biological therapy, elderly population, psoriasis, treatment

關鍵詞：生物治療、老年人口、銀屑病、治療

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Introduction

Psoriasis is a chronic inflammatory disease of unknown aetiology that affects 2% of the population. The life expectancy of patients with psoriasis is the same as that of the general population, hence its prevalence increases progressively with age. This makes the elderly population an important group in patients with psoriasis, and also means that the diagnosis, therapeutic management and knowledge of the different clinical forms of the disease are important not only to dermatologists but also to their families and the attending physicians.

Epidemiology

Epidemiological studies generally do not make a special assessment of the disease in the elderly population. The worldwide prevalence of psoriasis is approximately 2%, although there are important regional and ethnic group-specific variations. This is why genetics and/or environmental factors that have not been fully characterised may have an impact. There is a greater incidence in Caucasians, ranging from 1.5% in Croatia and most of the Mediterranean countries to 4.8% in Norway.¹

In Spain, the most extensive study included a sample of almost 13,000 subjects, being similar in both sexes, with an estimated prevalence of between 1.17% and 1.43%, being higher between the ages of 20 and 50 years with a greater predominance in the country's central regions. In this study, 1.44% of the patients were aged between 61 and 70 years and 0.33% of cases were more than 70 years old.² More recent studies in our country have assessed the psoriasis characteristics of elderly patients and concluded that this group of patients has a greater rate of hypertension, left ventricular hypertrophy, diabetes mellitus and insulin resistance. It is of interest to note that this study also indicates a greater severity of psoriasis in patients who are heavy drinkers and smokers.³

Life expectancy is currently around 85 years for women and 80 years for men. If these values continue to increase, the same will occur in the psoriatic population, leading to a greater burden in terms of the comorbidities, and also in terms of the adverse effects associated with the different treatments, drug interactions, poor health habits and cardiovascular risk factors.

Clinical particularities of psoriasis in the elderly patient

This article does not purport to review clinical symptoms and/or clinical forms in elderly patients,

although it might be interesting to highlight certain salient points regarding daily clinical practice and its repercussions on treatment.

First of all, it must be stressed that there are no fundamental differences in the form of clinical expression of psoriasis between the elderly and younger patients. We would also emphasise the following specific features:

- a) *Guttate psoriasis*. It does not affect the elderly and is almost exclusive to adolescents and young adults.
- b) *Inverse psoriasis* (axillae, skin folds between buttocks, popliteal fossae and skin folds under the breasts). Inverse psoriasis is more common in elderly patients, especially in the obese or people with associated comorbidities. Occasionally there are scales at the bottom of the fold, and the edge of the lesion is usually well-defined, which may be a distinguishing feature from other infectious forms of intertrigo. However, inverse psoriasis can also become super-infected and may require combined treatment for both conditions.
- c) *Nail psoriasis*. There are no differences in clinical symptoms, either in the nailbed or the matrix. Its incidence is possibly greater and is also associated with the greater prevalence of psoriatic arthropathy in the elderly. It should be considered in the differential diagnosis of other causes of onychodystrophy and nail symptoms that occur in normal nail ageing.
- d) *Scalp psoriasis*. This affects the occipital area more frequently. The associated pruritus tends to be greater in this location, probably caused by dry skin, giving rise to abundant serous bullae and crusts with lesions caused by Koebner phenomenon.

Comorbidities associated with psoriasis

In recent years, psoriasis has been shown to be much more than a skin disease. The concept of systemic inflammatory disease has gained support with time. There are a wide number of diseases

associated with psoriasis with a frequency that is higher than expected in the general population. The main diseases associated with psoriasis are:

- Psoriatic arthritis. The association between psoriasis and psoriatic arthropathy is variable but different studies have shown that 20% of patients aged over 65 years with psoriasis have associated arthropathy.⁴
- Cardiovascular disease and its associated risk factors (diabetes, obesity, hypertension, metabolic syndrome).⁵ Patients with chronic diseases are at a greater risk of metabolic syndrome (Table 1).
- Haematopoietic tumours, pancreatic cancer.⁶
- Autoimmune bullous diseases, mainly bullous pemphigoid.⁷
- Osteoporosis.^{8,9} There are conflicting reports on the association of osteoporosis and psoriasis. Some studies report an association between psoriasis and osteoporosis in males,⁵

while others have not found any significant difference.

- Anxiety and depression.¹⁰ Psoriasis is one of the inflammatory diseases of the skin that has a great impact on quality of life, similar to that of other systemic diseases (diabetes, cardiovascular diseases, cancer). The perception of rejection and isolation is the most commonly reported by all psoriasis sufferers and this aspect should not be neglected. Any of the relevant validated quality of life instruments—Skindex29 DLQI, PDI can be used to demonstrate the substantial difference with regard to younger patients.
- Inflammatory bowel disease.¹¹

Each case should be treated on an individual basis. The dermatologist is the most suitable specialist for early detection but the primary care doctor or an appropriate specialist should perform

Table 1. Metabolic syndrome diagnostic criteria

CRITERION	NCEP-ATP III	WHO	IDF
	3 or more of the following	Obligatory criterion* + 2 or more of the following	Obligatory criterion* + 2 or more of the following
FASTING GLUCOSE	FG 110-126 mg/dL	*Type 2 Diabetes, IR +/- GI	FG ≥/ = 100 mg/dL (5.6 mmol/L), or type 2 DM
OBESITY	Waist circumference >102 cm men >88 cm women	Waist-to-hip ratio >0.90 men >0.85 women BMI >30 kg/m ²	*Central Obesity: waist circumference ≥94 cm men ≥80 cm women
DYSLIPIDAEMIA	TG ≥150 mg/dL HDL cholesterol <40 mg/dL men <50 mg/dL women	TG ≥150 mg/dL HDL <35 mg/dL in men <39 mg/dL in women	TG ≥150 mg/dL HDL <40 mg/dL men <50 mg/dL women, or treatment
BLOOD PRESSURE	≥130/85	≥/ = 140/90 mmHg	SBP ≥130 DBP ≥85 mm Hg, or patient is controlled with treatment
OTHERS		Urinary albumin excretion >20 ug/min or albumin – creatinine ratio ≥/ = 30 mg/g	

NCEP-ATPIII: National Cholesterol Education Program Adult Treatment Panel III; WHO: World Health Organisation; IDF: International Diabetes Federation; FG: Fasting glucose; IR +/- GI: Insulin resistance ± glucose intolerance; TG= Triglycerides; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure

the relevant monitoring and treatment of any associated comorbidities.

Treatment of psoriasis in the elderly patient

General considerations

In pharmacology, old age begins at 65 years, and patients may be divided into three different age groups: a) 65-74 years, b) 75-84 years and c) above 85 years. This classification may be controversial due to the lack of concordance between physiological age and chronological age. What does seem clear is that the effects of age-related changes in pharmacokinetics are variable and difficult to predict. They are not only due exclusively to age, but also due to the presence of chronic diseases in these patients, polypharmacy, malnutrition and motor or cognitive impairment.¹²

Another factor to be taken into account is treatment compliance. While there are no sound studies on this issue, it is presumably lower in the geriatric population due to sensory deficits, dependence on relatives or caregivers or multiple other associated diseases that require intake of several drugs every day.

Before discussing the different topical, systemic and biological medicines in the geriatric population in detail, we agree with Tuneu in highlighting the application of some simple guidelines to minimise possible risks in the administration of any kind of medication in this patient category (Table 2).¹³

Topical treatment

Corticosteroids are still the first-line topical treatment, and their use is governed by the same criteria as in other dermatoses. The dose, potency and exposure time of the corticosteroid must be adjusted, and therapy rotated as necessary. It should not be forgotten that the skin of the elderly patient with psoriasis has probably undergone prolonged topical steroid treatment making tachyphylaxis more common. Also, since skin thinning due to ageing is often present, these patients are more prone to the side effects of continuous use of topical steroids (atrophy, stretch marks, capillary fragility). The reduction in skin thickness can also boost systemic absorption of the corticosteroid, and therefore the systemic effects derived from the suppression of the hypothalamic-pituitary-adrenal axis may be enhanced.

Table 2. Minimum precautions for avoiding drug interaction in the elderly population

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- Minimise the number of drugs in each patient and take possible interactions into account.
 - Before prescribing a drug, any physiological variation or pathological alteration that may affect dosage and the medicinal product's response should be taken into account.
 - The patient should be given the lowest possible dose, titrated according to response.
 - The form of administration and dosage should be as simple as possible.
 - The patient or caregiver should understand the guidelines. The treatment should be given in writing.
 - Make sure that patients' motor, visual and cognitive functions do not lead to errors or poor compliance.
 - Patients should be monitored closely to ascertain compliance, medication effectiveness and adverse effects.
 - Personal and economic conditions should be taken into account.
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The combination of calcipotriol and betamethasone is useful and effective in elderly patients, and sometimes achieves a better result than that in the younger population, with good treatment compliance and without an increase in adverse effects.¹⁴

The use of topical calcineurin inhibitors in off-label indications (mild and moderate-to-severe atopic dermatitis) has provided an interesting and efficacious alternative in the treatment of facial, genital and flexural psoriasis, while avoiding the side effects of prolonged topical corticosteroid use.¹⁵

Phototherapy

Data on phototherapy, both NBUVB and PUVA are limited in the elderly population. Although NBUVB has become more commonly used than PUVA therapy,¹⁶ some authors advocate reasonable use of phototherapy in patients who present with moderate-to-severe psoriasis after establishing a proper risk/benefit balance and regular monitoring for skin malignancy.

The main drawback is determining the person's capacity to remain standing for the necessary time during treatment, and the drawbacks derived from its administration, which is two to three times weekly. The benefits in female population may even be greater since it promotes the synthesis of vitamin D in postmenopausal women.¹⁷

Systemic therapy

Methotrexate (MTX)

Methotrexate is indicated as systemic treatment in moderate-to-severe plaque psoriasis, psoriatic erythrodermia, generalised pustular psoriasis, nail psoriasis, palmoplantar psoriasis and psoriatic arthritis. It may be used if there is of lack of response to topical treatment, acitretin, PUVA/NBUVB or if these are not available or not tolerated.

Methotrexate is usually administered in an intermittent low-dose regimen such as once weekly in daily clinical practice. Administration can be via oral or subcutaneous route. The usual dose range is between 7.5 mg and 15 mg per week. Higher doses are usually not necessary. Folic acid, 5-15 mg weekly, protects against some of the common side effects seen with low-dose methotrexate such as stomatitis. Patients without risk factors for hepatotoxicity should have liver function checked every one to three months. Liver biopsy should also be considered after a cumulative dose of 3.5 to 4 g. The main interactions are with NSAIDs.

It is an effective treatment in the elderly, although lower doses than those given to younger patients are recommended. This is why it is postulated as a relative contraindication in the usage guides recently published in Spain.¹⁸ From a practical point of view, the most important requirement is to monitor the blood count and liver function. In contrast to younger patients, procollagen type III aminoterminal peptide measured every three months is not as sensitive in detecting liver damage. Methotrexate may be reserved for rescue therapy during psoriatic flares instead of as first-line treatment if there is concern over the risk of cumulative toxicity.

Great care should be taken in renal failure patients as acute myelosuppression is more frequent in patients on MTX, and a test dose should be considered. Its use in this population is supported by the reported cardio-protective effect of MTX from many studies.¹⁹

Acitretin (ACI)

Acitretin is a first-line drug for pustular psoriasis, particularly the palmoplantar variant, and to establish long-term psoriasis treatment strategies in rotation, sequencing or combination. Due to its non-immunosuppressive action, ACI is recommended as a first-line systemic treatment in patients with melanoma,

solid and lymphoproliferative neoplasms and in patients with HIV infection. In the Spanish guidelines, paediatric and old age are regarded as relative contraindications.²⁰

The usual dose range of acitretin is 25 mg every other day to 50 mg daily. Most of the side effects are dose-dependent and well-tolerated at the recommended doses. Cutaneous xerosis is a limiting factor in the elderly population and therefore emollients are important. Other common side effects, especially seen in this age, include cheilitis and alopecia. Monitoring for hypertriglyceridaemia and hepatotoxicity are required with retinoid therapy. Acitretin is teratogenic so it is only indicated in men and in women of non-reproductive potential. Pregnancy is contraindicated for two years after discontinuing the drug. Adverse reactions are less frequently associated with lower doses (25 mg/d). However, the toxic dose is very close to the therapeutic dose, thus accounting for the presence of side effects during the initial period, while the dose is still being titrated. These effects are normally reversible when the dose is reduced or discontinued. With the photoageing of the elderly population in our country, its protective effect against photoageing and non-melanoma skin cancer makes acitretin a desirable treatment. However due to its potential photosensitive effect, a suitable sunscreen and sun protective measures are required. The absence of immunosuppression makes it a treatment of choice in the elderly population. However, hypertriglyceridaemia may require both dietary measures and pharmacological correction.¹⁶

Ciclosporin

Ciclosporin is widely used in the treatment of transplantation patients and also in some dermatological conditions such as atopic dermatitis, pyoderma gangrenosum and psoriasis. In the elderly population in our clinical practice it is rare to exceed the dose of 3 mg/kg/day and shorter treatment cycles are preferred. The initial daily dose of ciclosporin is usually 2.5 mg/kg in two divided doses. The dose can be increased to

a maximum of 4 mg/kg per day. Since ciclosporin is metabolised by hepatic cytochrome P4503A enzymes, a variety of important drug interactions with drugs metabolised by these enzymes can occur, e.g. diltiazem, nicardipine, verapamil, fluconazole, itraconazole and colchicine.

As well as nephrotoxicity which is one of its main side effects, there is a long term risk of carcinogenesis. Close monitoring for hypertension, a common condition in these patients is needed and often limits the long-term use of ciclosporin in elderly psoriatic patients. At present, there are no Spanish guidelines for the specific use of this agent in patients with psoriasis, but its use should be restricted or it should be used with great caution in patients with a baseline impairment of renal function or poorly controlled hypertension. These two problems are encountered with greater frequency in the elderly and may be regarded as relative contraindications. Ciclosporin should therefore be used as a second-line treatment or in cases requiring a rapid clearance of psoriasis.²¹

Biological therapy

The introduction of biologics has provided another treatment option for psoriasis patients who have not been able to tolerate or respond to conventional treatment modalities (Figures 1 & 2). In the elderly population, most studies agree that there is a similar efficacy of anti-TNF treatments in young and elderly patients. Elderly patients are not regularly included in clinical trials, hence there are no explicit recommendations in the guidelines on treatment or summaries of drugs for the treatment of moderate-to-severe psoriasis in this group.²²⁻²⁵ Dose adjustment is not usually required, although special caution is required as the incidence of severe infections in patients over 65 years old is greater than that in younger patients.

One of the representative studies is a systematic review from 2011 conducted by Busquets et al that assessed the efficacy and safety of anti-TNF

treatment in elderly patients.²⁶ It included 10 studies with a total of almost 5000 patients above the age of 65 years treated with anti-TNF for rheumatological diseases. It was concluded that the retrospective studies were not designed specifically to assess the elderly population (either efficacy or safety). The difference in efficacy between the young and elderly population was not significant. Although

the difference did not reach statistical significance, elderly people presented with a higher rate of adverse effects. However, there were more local site reactions, headache, rhinitis, allergic reactions and upper respiratory tract infections in the young subjects. These findings were also reported by other studies more focused on the elderly population, particularly with etanercept and adalimumab.^{27,28}



Figure 1. Moderate psoriasis with PASI > 10 pre-biological treatment (Etanercept).

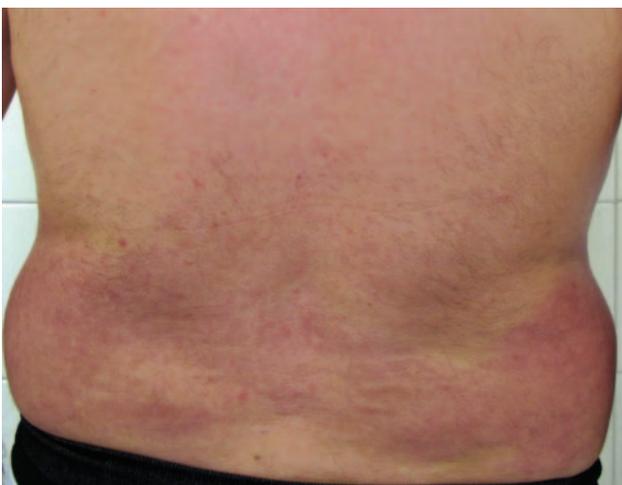


Figure 2. Control six months after biological treatment.

In view of the lack of evidence, expert consensus has been reached on the choice of treatment for psoriasis in the elderly. In an expert consensus, etanercept was the treatment of choice due to its shorter half-life in cases where patients need to be vaccinated or if treatment may be suspended due to surgery.²⁹

Conclusion

The management of psoriasis in elderly patients is a veritable challenge, due to the absence of specific data on the safety and efficacy of the different treatments available (Figure 3). However, treatment objectives should not vary substantially from the younger patients: disease control, fulfilling patient expectations, improving quality of life and seeking efficacious and safe treatment regimens. Further quality studies are called for in the management of psoriasis in our elderly patients.

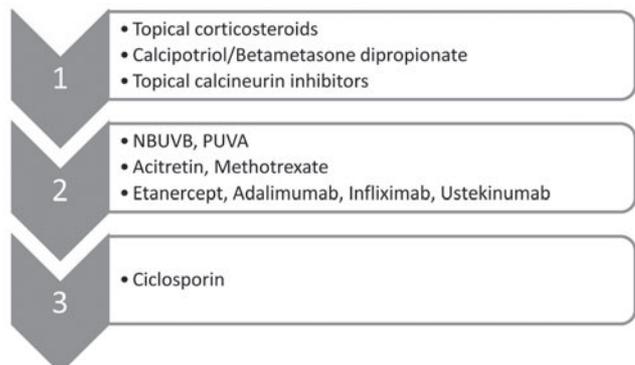


Figure 3. Treatment algorithm (based on Grozdev et al¹⁶).

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