



ARTICLE REVIEW

**Therapeutic Management of Moderate-Severe Psoriasis Associated with HIV Infection: A Literature Review**

Manejo terapéutico de la Psoriasis Moderada-Severa asociada a infección por VIH: Una Revisión Bibliográfica

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**ABSTRACT**

**Introduction:** psoriasis is a chronic skin disease that can affect any part of the body and cause itching, pain and discomfort, its severity varies from mild to severe and has a significant impact on the quality of life of those who suffer from it. Psoriasis in individuals with Human Immunodeficiency Virus presents particular challenges, manifesting itself in a more severe and treatment resistant manner.

**Objective:** to analyze the impact of treatments for psoriasis when HIV is present, identifying current trends in terms of efficacy, safety and possible drug-drug interactions, therapeutic relationship and its clinical implications.

**Methods:** analysis of original articles and systematic reviews previously carried out that provided information on the therapeutic management of moderate-severe psoriasis associated with HIV infection, in addition, the search for information from different databases such as Scielo, Elsevier, PubMed, Chrocrane, Epistemonikos and different journals including Seimc, Medigraphic Artemis, Recimundo, SCIENCE, MEDICRIT, etc. was prioritized.

**Results:** the importance of an integral therapeutic approach is emphasized, considering the immunodeficiency associated with the Virus. Treatment will focus on the various measures adopted when treating psoriasis, such as phototherapy, the use of oral retinoids and biological treatment, and we also consider that antiretroviral therapy is fundamental for the treatment of psoriasis.

**Conclusions:** the review provides a thorough investigation of current therapeutic strategies, highlighting the importance of adapting them to the complexity of HIV coinfection.

**Keywords:** Psoriasis; HIV; Phototherapy; Retinoids; Treatment.

## RESUMEN

**Introducción:** la psoriasis es una enfermedad crónica de la piel que puede afectar a cualquier parte del cuerpo y causar picazón, dolor e incomodidad, su gravedad varía de leve a grave y llega a tener un impacto significativo en la calidad de vida de quienes lo padecen. La psoriasis en individuos con Virus de Inmunodeficiencia Humana presenta desafíos particulares, manifestándose de manera más grave y resistente al tratamiento.

**Objetivo:** analizar el impacto de los tratamientos hacia la psoriasis cuando está el VIH presente, identificando las tendencias actuales en términos de eficacia, seguridad y posibles interacciones medicamentosas, relación terapéutica y sus implicaciones clínicas.

**Métodos:** análisis de artículos originales y revisiones sistemáticas previamente realizadas que aportaron con información sobre el Manejo terapéutico de la psoriasis Moderada-Severa asociada a infección por VIH, además se priorizó la búsqueda de información de diferentes bases de datos como Scielo, Elsevier, PubMed, Chrocrane, Epistemonikos y diferentes revistas entre ellas Seimc, Medigraphic Artemisa, Recimundo, SCIENCE, MEDICRIT

**Resultados:** se destaca la importancia de un enfoque terapéutico integral, considerando la inmunodeficiencia asociada al Virus. El tratamiento se enfocará en las diversas medidas que se adoptan al momento de tratar la psoriasis, como lo es la fototerapia el uso de retinoides orales y el tratamiento biológico, además consideramos que la terapia antirretroviral es fundamental para controlar la infección y puede influir en la evolución de la psoriasis.

**Conclusiones:** la revisión proporciona una exhaustiva investigación de las estrategias terapéuticas actuales, resaltando la importancia de adaptarlas a la complejidad de la coinfección VIH.

**Palabras Clave:** Psoriasis; VIH; Fototerapia; Retinoides; Tratamiento.

## INTRODUCTION

Psoriasis is a chronic, immune-mediated disease that affects between 1 % and 4 % of the adult population worldwide. It is considered a common inflammatory skin condition, has a predominant genetic basis and is linked to relevant medical and psychosocial comorbidities. Advances in the understanding of its pathophysiology have led to the development of an increasing number of therapeutic options, offering the possibility of significantly improving the quality of life of those who suffer from this disease. The incidence of psoriasis ranges between 1 % and 3 % globally. However, in certain countries, this figure can fluctuate between 0,09 % and 11,4 %, depending on factors such as age, ethnic origin, gender and geographic location.<sup>(1)</sup>

Psoriasis in individuals with human immunodeficiency virus (HIV) infection is associated with increased immunodeficiency and typically manifests when CD4 cell counts have dropped below 100 cells/microliter.<sup>(2)</sup>

The severity of psoriasis is assessed by the extent and impact of the skin lesions, and other factors such as the impact on the patient's daily activities and symptoms such as pain or itching. Generally speaking: Mild Psoriasis: Lesions are few and localized to limited areas of the body. Moderate Psoriasis: Lesions cover a larger portion of the body, but are not as widespread. Moderate to Severe Psoriasis: In this category, lesions are more extensive and may affect major areas of the body. In addition, symptoms may be more pronounced, and the condition may have a significant impact on the patient's quality of life. Severe Psoriasis: Psoriasis is extensive, affects

multiple areas of the body, and can have a significant impact on the individual's overall health and well-being.<sup>(3)</sup>

HIV infection weakens the immune system, culminating in acquired immunodeficiency syndrome (AIDS). This impairment increases susceptibility to diseases such as tuberculosis and infections, as well as certain types of cancer. Transmission occurs through bodily fluids, excluding everyday gestures. Antiretroviral treatment (ART) controls and prevents the infection, avoiding its progression to AIDS, identified by the WHO in adults and adolescents in stages three or four, or when the CD4 cell count is less than 200 per mm<sup>3</sup>.<sup>(4)</sup>

The prevalence of HIV-associated psoriasis may range from 2,5 % to 5 %. Psoriasis may present as the first cutaneous sign of HIV infection and persists throughout all stages of the disease, including acquired immunodeficiency syndrome (AIDS). HIV-associated psoriasis tends to appear around age 30, and approximately 90 % of patients with HIV-AIDS experience some skin disorder. In those who develop AIDS, psoriasis tends to be more severe, resistant to treatment, and predominantly localized to acral or generalized areas. The most common types of psoriasis associated with HIV-AIDS include vulgaris, guttate, and erythrodermic psoriasis.

Psoriasis can worsen in patients with the human immunodeficiency virus (HIV). Treatments are divided into three main parts, with phototherapy being one of the most prominent. This modality contributes to reducing the growth of skin cells and addressing inflammation; Second-line therapy consists of oral retinoids as monotherapy or in combination and as a third line we have biological treatment where the focus is on tumor necrosis factors (TNF) and interleukins (IL). We also consider antiretrovirals since they are effective in treating HIV-related psoriasis, especially in cases of sudden outbreaks or resistance to therapy.<sup>(5,6)</sup>

Treating psoriasis in HIV-infected individuals poses a significant therapeutic challenge, as it involves a T-cell-mediated disease in a setting characterized by T-cell exhaustion. Addressing moderate to severe HIV-associated psoriasis is challenging, although highly effective antiretroviral therapy often improves patients' condition.

It is important to note that conventional systemic treatments may be contraindicated or require dosage adjustments to prevent toxicity. In this context, new biological treatments are presented as promising options and deserve further investigation. Both conventional systemic and biological agents can be considered. Furthermore, regular monitoring of CD4 counts and HIV viral loads is required to ensure adequate management of psoriasis and minimize risks associated with HIV infection.<sup>(7,8,9,10)</sup>

All of the above leads us to ask the following question: What is the impact of psoriasis treatments when HIV is present; current trends in terms of efficacy, safety and possible drug interactions, therapeutic relationship and its clinical implications? Hence, the objective is to analyze the impact of psoriasis treatments when HIV is present, identifying current trends in terms of efficacy, safety and possible drug interactions, therapeutic relationship and its clinical implications.

## METHODS

A bibliographic review was carried out in which the analysis of original articles and previously carried out systematic reviews was executed that provided information on the therapeutic management of moderate-severe psoriasis associated with HIV infection. In addition, priority was given to the search for information from different databases such as Scielo, Elsevier, PubMed, Chrocrane, Epistemonikos and different journals including Seimc, Medigraphic Artemisa, Recimundo, SCIENCE, MEDICRIT, articles published from 2020 to March 2024, using the following keywords: Psoriasis, HIV, Phototherapy, Retinoids, Treatment.

The main keywords Psoriasis, HIV, Phototherapy, Retinoids, Treatment were searched individually and the search was subsequently repeated in association with each of the secondary keywords. Papers not suitable for the purpose of the review were excluded. Articles were independently selected by two co-authors and their subsequent selection was unanimous and collaborative.

## DEVELOPMENT

The treatment of moderate-severe psoriasis associated with HIV is based on three therapeutic pillars. The first line includes phototherapy with narrow band ultraviolet B light (UVB) which acts as a photosensitizer followed by ultraviolet A radiation (UVA), which clinically exert antiproliferative and anti-inflammatory effects since they induce apoptosis of T cells. It is recommended to administer three times a week and once the lesions have reduced, minimal doses are administered.<sup>(11)</sup>

In pregnancy, patients with psoriasis who are infected with HIV often experience exacerbations and a lower response to treatment, and there is not enough evidence for the treatment of psoriasis in pregnant women with HIV.<sup>(12)</sup> In this case, the use of topical glucocorticoids is initially indicated, but in the case of HIV, treatment with ultraviolet (UV) light phototherapy, specifically narrow-band UVB-BE ultraviolet radiation, will be started. "UV light therapy is considered safe during pregnancy," according to Balakirski. However, folic acid levels may be negatively affected. Therefore, these patients should take the standard dose of 0.8 mg of folic acid per day.<sup>(13)</sup>

Narrowband ultraviolet B light phototherapy, which should be administered two to three times a week, where improvement must be seen after approximately 20 to 30 treatments or it is considered a failure.<sup>(14)</sup>

Phototherapy is considered safe for use in patients with HIV-associated psoriasis when administered in conjunction with antiretroviral therapy. However, caution is required with its use, as it may have carcinogenic potential and worsen immunosuppression. The existence of Kaposi's sarcoma contraindicates the use of phototherapy in HIV-positive patients, and caution should be exercised in patients with darker skin phototypes, as they require higher doses of phototherapy, which may increase their immunosuppression and viral load.<sup>(15)</sup>

Antiretroviral therapy (ART) should be considered as first-line therapy, since it prevents the appearance of multisystemic signs and symptoms and delays the appearance of skin lesions once HIV is diagnosed, such as zidovudine, which has an antipsoriatic effect, which is due to interference with DNA synthesis by decreasing keratinocyte proliferation. Doses of 500-600 mg/day administered in two or three doses are recommended.<sup>(16,17)</sup>

For the second line, monotherapy with retinoids that exert anti-inflammatory and immunomodulatory effects is recommended as a systemic treatment for moderate to severe HIV-related psoriasis, such as acitretin at initial doses of 25-30 mg orally for two to four weeks. Combined therapy with retinoids with psoralen plus ultraviolet A (UVA) radiation is also recommended, showing better tolerance and less exposure to ultraviolet rays.<sup>(18)</sup> Common side effects of topical treatments include hypopigmentation, skin atrophy, and striae. In addition, there are contraindications for their use in cases of rosacea, acne vulgaris, perioral dermatitis, and skin infections. It has also been observed that these treatments may worsen pathologies such as HIV. It is important to note that the side effects of topical treatments in HIV patients are similar to those in the non-HIV-infected population, which underscores the need for special care when using these agents in this group of patients.<sup>(19)</sup>

The third line of treatment focuses on refractory patients and therapy includes immunosuppressants such as methotrexate, cyclosporine and hydroxyurea. Although methotrexate is a key drug in the treatment of HIV-associated psoriasis, it is hepatotoxic and nephrotoxic, so doses of 5-25 mg weekly are recommended depending on renal and hepatic function. Most side effects are dose-related and are generally well tolerated when administered at the recommended doses. Adverse reactions, both clinical and laboratory, are less frequent at low doses than at high doses. However, the toxic dose is very close to the therapeutic dose, meaning that most patients experience some side effects during the initial period while the dose is being adjusted.<sup>(20)</sup>

Cyclosporine acts by inhibiting calcineurin, which leads to blocking the inflammatory chain. This systemic drug is rapidly absorbed and complete remission is achieved within a few months of starting treatment. The recommended dose is 2,5 - 5 mg/kg/day for a period of two to four weeks.<sup>(17,18)</sup>

Hydroxyurea is an immunomodulator that has a dual antipsoriatic and antiviral effect by inhibiting the ribonucleotide reductase enzyme involved in DNA synthesis in the S phase, thereby reducing the proliferation of skin cells, controlling the symptoms of psoriasis. In addition, by inhibiting the immune system, it controls the inflammatory response and abnormal cell proliferation associated with psoriasis; Side effects include low blood counts, constipation, mouth and lip sores, pain or difficulty urinating, confusion, dizziness, hallucinations. It has antioxidant properties, which means it helps protect skin cells, where oxidative stress contributes to inflammation. It is used as an alternative to replace methotrexate in cases of liver cirrhosis and the recommended dose is 500 mg to 1000 mg per day, administered in one or two divided doses.<sup>(21)</sup>

And biological drugs such as risankizumab and guselkumab, selective inhibitors of the p19 subunit of IL-23, prevent the risk of infections by intracellular pathogens and are highly effective with PASI responses.<sup>(22)</sup> Risankizumab doses of 150 mg (two 75 mg injections) administered by subcutaneous injection at weeks 0 and 4 and every 12 weeks thereafter are recommended.<sup>(23)</sup> And guselkumab dose of 100 mg by subcutaneous injection at weeks 0 and 4, followed by a maintenance dose every 8 weeks.<sup>(24)</sup>

Psoriasis, a chronic inflammatory skin disease with a genetic basis, affects a significant percentage of the world's population. Its implications go beyond cutaneous manifestations, as it is associated with relevant medical and psychosocial comorbidities. The relationship between psoriasis and HIV infection adds an additional layer of complexity, as psoriasis in HIV patients tends to be more severe and resistant to treatment.

In this context, it is essential to understand the interaction between psoriasis and HIV, as well as to assess efficacy. The incidence of psoriasis varies significantly globally, and the presence of HIV may increase the prevalence of psoriasis in certain patient groups. The relationship between psoriasis and HIV becomes more evident in patients with immunodeficiency, especially when CD4 lymphocyte levels decrease below 100 cells/microliter. The decrease in CD4 lymphocytes in HIV patients contributes to the complexity and severity of psoriasis by affecting the immune response and the body's ability to control skin inflammation. This highlights the importance of addressing psoriasis in HIV patients in a comprehensive manner, considering compromised immune function and adapting therapeutic approaches accordingly.

HIV-associated psoriasis tends to manifest around age 30, and its presence persists throughout all stages of HIV infection, including acquired immunodeficiency syndrome (AIDS). The therapeutic approach to psoriasis in HIV-infected individuals poses considerable challenges due to T-cell mediation in an environment characterized by decreased T-cell counts. Although antiretroviral therapy (ART) has been shown to improve the condition of HIV-infected patients, conventional systemic treatments may be contraindicated or require dose adjustments to avoid toxicity. In this regard, biological treatments emerge as promising options.

A comprehensive search of the updated scientific literature revealed several therapeutic lines to address moderate-severe HIV-associated psoriasis. Phototherapy, particularly with narrowband ultraviolet B (UVB) light or psoralen-based ultraviolet light (PUVA), is presented as a first-line option, with antiproliferative and anti-inflammatory effects. Antiretroviral therapy, as a fundamental part of treatment, not only controls HIV infection but also delays the appearance of psoriatic skin lesions. Specific antiretroviral drugs, such as zidovudine, show antipsoriatic effects by interfering with DNA synthesis and reducing keratinocyte proliferation.

The second line of therapy involves oral or topical retinoids, with evidence of anti-inflammatory and immunomodulatory effects. The combination of retinoids with phototherapy shows better tolerance and less exposure to ultraviolet rays.

The third line is reserved for refractory patients and includes immunosuppressants such as methotrexate, cyclosporine, hydroxyurea and biologic drugs such as risankizumab and guselkumab. The identification of these therapeutic options provides a comprehensive view on how to address psoriasis in patients with HIV, considering efficacy, safety and possible drug interactions.

For pregnant patients, treatment initially includes topical corticosteroids, but HIV infection requires starting with phototherapy treatment with narrow-band ultraviolet B radiation. There is not much evidence of good results, but this would be the responsibility of the person in charge through clinical judgment. This lack of solid scientific evidence underlines the urgent need to carry out more research in this area. Given the complexity and importance of ensuring the safety and efficacy of treatments in this group of patients, it is crucial that more longitudinal studies are carried out to fill this knowledge gap and provide evidence-based guidelines for the clinical management of psoriasis in pregnant women with HIV.

It is crucial to highlight the importance of regular monitoring of CD4 counts and HIV viral loads to adequately manage psoriasis and minimize the risks associated with HIV infection. In summary, our literature review highlights the complexity of the relationship between psoriasis and HIV, as well as the diversity of therapeutic options available. Understanding these interactions is essential to improve the quality of life of patients and to provide a comprehensive and updated approach to the management of this dermatological condition in the context of HIV infection.

We conclude by expressing psoriasis primarily as a chronic inflammatory disease, with variations according to factors such as age, ethnicity, gender and geographic location. The incidence of HIV-associated psoriasis can range from 2,5 % to 5 %, being more severe, resistant to treatment and predominantly localized in acral or generalized areas in patients with HIV-AIDS. Treatment of HIV-associated psoriasis poses significant challenges due to T-cell-mediated disease in an immunodeficiency setting. Treatments include phototherapy, antiretroviral therapy, immunosuppressive retinoids and biologic drugs. Retinoids, cyclosporine, methotrexate, hydroxyurea and biologic drugs are reserved for refractory cases, showing variable efficacy and safety considerations.

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