ISSN 2664-8075 (Print) & ISSN 2706-5774 (Online)
South Asian Research Journal of Applied Medical Sciences
Abbreviated Key Title: South Asian Res J App Med Sci

| Volume-7 | Issue-1 | Jan-Feb- 2025 | **DOI: https://doi.org/10.36346/sarjams.2025.v07i01.004**

Review Article

Drug-induced Psoriasis. A Review of the Literature

Vianca Andrea Ramírez-Hernández[1*]

[1]Hospital Regional de Alta Especialidad, Bicentenario de la Independencia. ISSSTE

***Corresponding Author:** Vianca Andrea Ramírez-Hernández
Hospital Regional de Alta Especialidad, Bicentenario de la Independencia. ISSSTE

Article History
Received: 11.01.2025
Accepted: 14.02.2025
Published: 26.02.2025

Abstract: Psoriasis is a chronic inflammatory skin disease with a complex and multifactorial pathophysiology. Among the triggering factors, certain medications have been implicated as causing the appearance of new cases or exacerbations in previously diagnosed patients. This article reviews the latest evidence on medications associated with induced psoriasis, paradoxical eruptions, the pathophysiological mechanisms involved, and clinical implications. Strategies for its management and prevention are also discussed, highlighting the importance of pharmacovigilance in these patients.

Keywords: Psoriasis, drug-induced diseases, drugs.

INTRODUCTION

Psoriasis is a chronic systemic disease that affects approximately 2-3% of the global population. Its clinical presentation includes various forms, such as plaque psoriasis, pustular, erythrodermic, and guttate psoriasis, each with specific characteristics. While genetic and environmental factors play a fundamental role, the relationship between certain medications and the exacerbation or induction of psoriasis has attracted increasing attention.

Among the drugs involved are beta-blockers, antimalarials, lithium, TNF-α inhibitors, and certain targeted therapies used in oncology. These drugs can act as triggers in genetically predisposed individuals or sensitize an already altered immune system, promoting uncontrolled inflammatory responses. The aim of this article is to review the pharmacological agents related to drug-induced psoriasis and the biological mechanisms underlying this phenomenon.

METHODOLOGY

A search was conducted in biomedical databases such as PubMed, Scopus, and Web of Science. The terms used included "drug-induced psoriasis," "medication-exacerbated psoriasis," "psoriasis induced by drugs," and "pityriasis pathophysiology." Inclusion criteria covered original articles, clinical case reports, and systematic reviews published between 1996 and 2024 in English and Spanish. Animal model studies, duplicates, and those not focused on specific medications were excluded. Cohort studies, systematic reviews, and case reports with a detailed description of the implicated drugs, clinical phenotypes, and potential immunological mechanisms were prioritized.

RESULTS

- Beta-blockers: Frequently reported to exacerbate psoriasis or induce psoriasiform eruptions. Although multiple studies support this association, the exact mechanism remains unclear.
- Lithium: Widely recognized for its potential to exacerbate psoriasis, lithium can induce psoriatic lesions even in individuals with no prior history of the disease. The mechanism is believed to involve the modulation of intracellular signaling pathways that affect keratinocyte proliferation [1-4].
- Antimalarials: Drugs such as hydroxychloroquine are known to trigger psoriasis, particularly in patients with pre-existing disease. They generally do not induce de novo psoriasis but can exacerbate latent psoriasis [1, 2, 4].

- Nonsteroidal anti-inflammatory drugs (NSAIDs): These are associated with exacerbations of psoriasis, although the evidence is less solid compared to other classes of medications. The mechanism could involve alterations in prostaglandin synthesis, which may affect inflammatory pathways [1, 2, 5].
- Anti-tumor necrosis factor (TNF) agents: Paradoxically, although these agents are used to treat psoriasis, they have been reported to induce de novo psoriasis in some patients. This paradoxical effect is believed to be related to the modulation of the immune system [1].
- Antihypertensives: Beyond beta-blockers, other antihypertensive agents such as ACE inhibitors, calcium channel blockers, and thiazide diuretics have been associated with psoriasis. The evidence suggests a potential risk, although the mechanisms are not fully understood [5, 6].

Beta-blockers

Beta-blockers are known to induce or exacerbate psoriasis, particularly vulgar psoriasis, in some patients. The literature indicates that the risk of psoriasis associated with beta-blocker use is statistically significant, with an odds ratio reported as 8.95, suggesting a strong pharmacovigilance signal [6]. The onset of psoriatic conditions after exposure to beta-blockers typically occurs within five months and often improves after discontinuation of the medication [6]. A systematic review and meta-analysis confirmed the association between beta-blockers and an increased risk of psoriasis, with a combined odds ratio of 1.40 [7]. Furthermore, long-term use of beta-blockers, particularly for six years or more, has been associated with a higher risk of developing psoriasis, as demonstrated in a prospective cohort study [8]. However, some studies did not find a significant association between beta-blocker use and the risk of psoriasis, indicating some inconsistency in the data [9].

In clinical practice, it is important to monitor patients with psoriasis who are receiving beta-blockers, especially during the first year of treatment, as this is the period when the risk of exacerbation or the appearance of new cases is most pronounced [6]. If psoriasis worsens, alternative antihypertensive therapies may be considered.

Lithium

Lithium is known to exacerbate psoriasis, particularly vulgar psoriasis and pustular psoriasis, in patients with bipolar disorder. The literature indicates that lithium can cause a variety of cutaneous adverse effects, with psoriasis being a significant concern. Its pathogenesis involves the influence of lithium on the cytokine network related to psoriasis, including modulation of cytokines such as IL-2, IL-6, IL-8, IFN-gamma, and TGF-alpha. These cytokines are involved in the hyperproliferation of keratinocytes and the dense infiltration of mononuclear cells characteristic of psoriatic lesions [10]. The prevalence of cutaneous reactions, including psoriasis, in patients treated with lithium can reach up to 45%, with men being more susceptible than women [11]. The exacerbation of psoriasis during lithium treatment has been documented in clinical reports, highlighting the need for careful monitoring of skin conditions in patients undergoing this therapy [12]. Management of lithium-induced psoriasis often involves continuing lithium treatment while addressing the skin condition; however, it may be necessary to discontinue the treatment in cases resistant to therapy.

Antimalarials

Antimalarial drugs, such as hydroxychloroquine and chloroquine, are known to exacerbate pre-existing psoriasis, especially in patients with conditions such as systemic lupus erythematosus (SLE) or psoriatic arthritis. The literature indicates that antimalarials do not induce de novo psoriasis, but they can trigger or worsen existing psoriasis. This exacerbation is believed to occur through a pharmacological mechanism involving the inhibition of transglutaminase activity, which affects epidermal proliferation and can trigger psoriatic flare-ups in predisposed individuals [13,14]. In patients with SLE or psoriatic arthritis, the use of antimalarials should be carefully considered, weighing the benefits of controlling the underlying autoimmune condition against the risk of exacerbating psoriasis. The decision to use antimalarials in these patients should be individualized, with close monitoring recommended to detect potential psoriatic flare-ups [13,14]. If psoriasis worsens significantly, it may be necessary to discontinue the antimalarial and explore alternative treatments.

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

The potential of nonsteroidal anti-inflammatory drugs (NSAIDs) to induce or exacerbate psoriasis is a topic of interest in the medical literature. According to a cohort study conducted by Wu *et al.*, there is evidence suggesting that prolonged use of NSAIDs may be associated with an increased risk of developing psoriatic arthritis (PsA), although the study did not find a clear association between NSAID use and the risk of psoriasis itself. This study emphasizes the importance of monitoring patients on long-term NSAID therapy for signs of PsA.

Additionally, research conducted by Arasa *et al.*, suggests that NSAIDs, such as indomethacin, could exacerbate psoriasis by influencing the inflammatory response in psoriatic skin. The study found that psoriatic fibroblasts have defective COX-2 induction, leading to altered immune responses that could worsen psoriasis [15]. This offers a mechanistic view of how NSAIDs may influence the pathophysiology of psoriasis.

Overall, while there is some evidence suggesting that NSAIDs could exacerbate psoriasis or increase the risk of PsA, the relationship is not fully established, and further research is needed to clarify these associations. Clinicians should be aware of these potential risks and consider them when prescribing NSAIDs to patients with psoriasis or a predisposition to psoriatic conditions.

TNF Inhibitors

The relationship between tumor necrosis factor (TNF) inhibitor therapy and the induction of psoriasis is a well-documented paradoxical adverse effect. TNF inhibitors, which are effective in treating various immune-mediated inflammatory diseases, including psoriasis, can paradoxically induce psoriasis in some patients. This phenomenon has been observed in different patient populations, such as those with inflammatory bowel disease (IBD), rheumatoid arthritis (RA), and juvenile idiopathic arthritis (JIA).

Several studies have highlighted this association. A nationwide cohort study in Denmark found that patients treated with TNF inhibitors had a higher risk of developing de novo psoriasis compared to those receiving conventional therapy, with a risk ratio of 2.12 for non-pustular psoriasis and 6.50 for pustular psoriasis [16]. Similarly, a study in children with IBD and JIA reported increased incidence rates of psoriasis in those treated with TNF inhibitors, with adalimumab showing a particularly high incidence rate [17]. Another study based on data from the Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry found nearly a threefold increase in the risk of psoriasis in children with JIA exposed to TNF inhibitors.

The exact mechanism behind TNF inhibitor-induced psoriasis is not fully understood, but it is hypothesized to involve alterations in cytokine profiles and modulation of the immune system. Despite this risk, the absolute incidence of TNF inhibitor-induced psoriasis remains relatively low, and the benefits of these drugs in managing underlying inflammatory diseases usually outweigh the risks of this adverse effect.

As for nonsteroidal anti-inflammatory drugs (NSAIDs), while they are known to exacerbate psoriasis, the link between prolonged NSAID use and the development of psoriatic arthritis is less clear and not directly addressed in the aforementioned literature. However, it is recognized that NSAIDs can worsen existing psoriasis in some patients, which may complicate the management of psoriatic arthritis.

In summary, while TNF inhibitors may induce psoriasis, the decision to use these agents should consider the overall clinical context, balancing the benefits in controlling the primary inflammatory disease with the risk of inducing psoriasis.

Antihypertensives

Antihypertensive medications have been associated with the induction or exacerbation of psoriasis, although the evidence is somewhat variable. A systematic review and meta-analysis found significant associations between several classes of antihypertensive drugs and the incidence of psoriasis. Specifically, angiotensin-converting enzyme inhibitors (ACE inhibitors), beta-blockers, calcium channel blockers (CCBs), and thiazide diuretics were associated with an increased risk of psoriasis, with odds ratios (OR) ranging from 1.40 to 1.70 [18]. This suggests that these medications could contribute to the development or worsening of psoriasis in some patients.

In contrast, a prospective cohort study from the Nurses' Health Study indicated that long-term hypertension itself is associated with an increased risk of psoriasis, and among antihypertensive medications, only prolonged use of beta-blockers (≥6 years) showed a significant association with psoriasis (hazard ratio [HR] 1.39) [19]. This study did not find a significant association between other antihypertensive drugs and psoriasis.

The Joint AAD-NPF Guidelines also recognize the potential of certain antihypertensive medications, particularly beta-blockers and ACE inhibitors, to exacerbate psoriasis, though they note that the evidence primarily comes from case reports and observational studies.

Overall, while there is evidence supporting the association between certain antihypertensive medications and psoriasis, the strength and consistency of these associations vary across studies. Physicians should be aware of these potential risks and monitor patients using these medications for signs of psoriasis.

Other Medications

Tetracyclines, a class of antibiotics, have occasionally been reported as associated with the worsening or induction of psoriasis, though the evidence is less robust compared to other medications such as lithium and synthetic antimalarials. The medical literature suggests that tetracyclines are among the drugs occasionally linked to the exacerbation or induction of psoriasis, but they do not present as strong a causal relationship as lithium and synthetic antimalarials.

CONCLUSION

Drug-induced psoriasis is a complex clinical entity that underscores the interaction between genetic predisposition and environmental factors. Early recognition and modification of the therapeutic regimen are essential to minimize the impact on the patient's quality of life. Further longitudinal studies are needed to fully understand the mechanisms and develop effective preventive strategies.

REFERENCES

1. Grželj, J., & Sollner Dolenc, M. (2020). The role of xenobiotics in triggering psoriasis. *Archives of Toxicology*, *94*(12), 3959-3982. doi:10.1007/s00204-020-02870-8.
2. Basavaraj, K. H., Ashok, N. M., Rashmi, R., & Praveen, T. K. (2010). The role of drugs in the induction and/or exacerbation of psoriasis. *International journal of dermatology*, *49*(12), 1351-1361. doi:10.1111/j.1365-4632.2010.04570.x.
3. Tsankov, N., Angelova, I., & Kazandjieva, J. (2000). Drug-induced psoriasis: recognition and management. *American journal of clinical dermatology*, *1*, 159-165. doi:10.2165/00128071-200001030-00003.
4. Fry, L., & Baker, B. S. (2007). Triggering psoriasis: the role of infections and medications. *Clinics in dermatology*, *25*(6), 606-615. doi:10.1016/j.clindermatol.2007.08.015.
5. Elmets, C. A., Leonardi, C. L., Davis, D. M., Gelfand, J. M., Lichten, J., Mehta, N. N., ... & Menter, A. (2019). Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with awareness and attention to comorbidities. *Journal of the American Academy of Dermatology*, *80*(4), 1073-1113. doi:10.1016/j.jaad.2018.11.058.
6. Azzouz, B., De Guizelin, A., Lambert, A., Fresse, A., Morel, A., & Trenque, T. (2022). Psoriasis risk after beta-blocker exposure: Description of a pharmacovigilance signal. *British Journal of Clinical Pharmacology*, *88*(8), 3813-3818. doi:10.1111/bcp.15330.
7. Song, G., Yoon, H. Y., Yee, J., Kim, M. G., & Gwak, H. S. (2022). Antihypertensive drug use and psoriasis: a systematic review, meta-and network meta-analysis. *British Journal of Clinical Pharmacology*, *88*(3), 933-941. doi:10.1111/bcp.15060.
8. Wu, S., Han, J., Li, W. Q., & Qureshi, A. A. (2014). Hypertension, antihypertensive medication use, and risk of psoriasis. *JAMA dermatology*, *150*(9), 957-963. doi:10.1001/jamadermatol.2013.9957.
9. Brauchli, Y. B., Jick, S. S., Curtin, F., & Meier, C. R. (2008). Association between beta-blockers, other antihypertensive drugs and psoriasis: population-based case–control study. *British journal of dermatology*, *158*(6), 1299-1307. doi:10.1111/j.1365-2133.2008.08563.x.
10. Ockenfels, H. M., Wagner, S. N., Keim-Maas, C., Funk, R., Nussbaum, G., & Goos, M. (1996). Lithium and psoriasis: cytokine modulation of cultured lymphocytes and psoriatic keratinocytes by lithium. *Archives of dermatological research*, *288*, 173-178. doi:10.1007/BF02505220.
11. Yeung, C. K., & Chan, H. H. L. (2004). Cutaneous adverse effects of lithium: epidemiology and management. *American journal of clinical dermatology*, *5*, 3-8. doi:10.2165/00128071-200405010-00002.
12. Skott, A., Mobacken, H., & Starmark, J. E. (1977). Exacerbation of psoriasis during lithium treatment. *British journal of dermatology*, *96*(4), 445-448. doi:10.1111/j.1365-2133.1977.tb07142.x.
13. Wolf, R., & Ruocco, V. (1999). Triggered psoriasis. *Rheumaderm: Current Issues in Rheumatology and Dermatology*, 221-225. doi:10.1007/978-1-4615-4857-7_32.
14. [14] Food and Drug Administration. Plaquenil. 2022.
15. Arasa, J., Terencio, M. C., Andrés, R. M., Marín-Castejón, A., Valcuende-Cavero, F., Payá, M., & Montesinos, M. C. (2019). Defective induction of COX-2 expression by psoriatic fibroblasts promotes pro-inflammatory activation of macrophages. *Frontiers in immunology*, *10*, 536. doi:10.3389/fimmu.2019.00536.
16. Thein, D., Egeberg, A., Skov, L., & Loft, N. (2022). Absolute and relative risk of new-onset psoriasis associated with tumor necrosis factor-α inhibitor treatment in patients with immune-mediated inflammatory diseases: a Danish Nationwide cohort study. *JAMA dermatology*, *158*(9), 997-1004. doi:10.1001/jamadermatol.2022.2360.
17. Baggett, K., Brandon, T. G., Xiao, R., Valenzuela, Z., Buckley, L. H., & Weiss, P. F. (2022). Incidence rates of psoriasis in children with inflammatory bowel disease and juvenile arthritis treated with tumor necrosis factor inhibitors and disease-modifying antirheumatic drugs. *The Journal of Rheumatology*, *49*(8), 935-941. doi:10.3899/jrheum.211359.
18. Song, G., Yoon, H. Y., Yee, J., Kim, M. G., & Gwak, H. S. (2022). Antihypertensive drug use and psoriasis: a systematic review, meta-and network meta-analysis. *British Journal of Clinical Pharmacology*, *88*(3), 933-941. doi:10.1111/bcp.15060.
19. Wu, S., Han, J., Li, W. Q., & Qureshi, A. A. (2014). Hypertension, antihypertensive medication use, and risk of psoriasis. *JAMA dermatology*, *150*(9), 957-963. doi:10.1001/jamadermatol.2013.9957.