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Pruritus in Psoriatic Patients: A Review Article

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ABSTRACT

Background: Psoriasis, a chronic skin condition, often accompanies distressing pruritus, impacting patients' quality of life. Understanding the pathogenesis of pruritus in psoriasis offers promising avenues in psoriasis treatment.

Objective: This review aimed to comprehensively explore the epidemiology, pathogenesis, clinical characteristics, impact on patients' quality of life, and treatment options associated with pruritus in psoriasis.

Methods: We searched Google Scholar, Science Direct, PubMed and other online databases for Psoriasis, Pruritus and Quality of life. The authors also reviewed references from pertinent literature, however only the most recent or comprehensive studies from 2012 to 2023 were included. Documents in languages other than English were disqualified due to lack of translation-related sources. Papers such as unpublished manuscripts, oral presentations, conference abstracts, and dissertations that were not part of larger scientific studies were excluded.

Conclusions: Pruritus is a prevalent and distressing symptom in psoriasis, affecting a majority of individuals with the condition.

Keywords: Psoriasis, Pruritus, Therapeutic interventions, Neuroinflammatory pathways.

INTRODUCTION

Psoriasis, a condition characterized by heightened keratinocyte growth, is a complex inflammatory skin ailment with both genetic and non-genetic roots. Factors contributing to its onset range from medications and smoking to stress, trauma, and various infections. This condition exhibits diverse forms, with plaque psoriasis being the most common. It results in raised, dry and red skin patches covered by silvery scales. Additional variations include nail psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis, erythrodermic psoriasis, and psoriatic arthritis [1].

For individuals grappling with psoriasis, pruritus, or itching, is a prevalent issue, affecting a substantial 70-90% of patients. This symptom significantly impacts their overall quality of life and often correlates with depressive symptoms, making it a particularly distressing aspect of the condition [2].

The underlying mechanisms of psoriasis involve a cascade of factors including excessive skin cell growth, heightened display of antigens, the production of specific T helper 1 cytokines, expansion of T-cells, and the formation of new blood vessels. Pruritus, commonly associated with dry skin or eczema, can also emerge from diverse conditions such as cirrhosis, blood disorders, infections, reactions to medications, and malignancies [3].

Pruritus in autoimmune and inflammatory dermatoses, is a common symptom that can be severe and affects patient's lifestyle. In some diseases, pruritus is related to disease activity and severity or may occur independently of the disease condition [4].

Pruritus has been linked to reduce quality of life and accompanies several skin disorders including burns, insect bites, xerosis, and dermatitis [5].

The purpose of this review was to provide a comprehensive overview of the current knowledge regarding the epidemiology, pathogenesis, clinical characteristics, impact on patients' quality of life, and treatment options associated with pruritus in psoriasis.

Psoriasis

Psoriasis, a prevalent chronic skin disease affecting individuals globally and spanning all ages, imposes a significant societal and personal burden. Linked to conditions like depression, psoriatic arthritis, and cardiometabolic syndrome, it manifests as erythematous papules and plaques with silver scales, often manageable in outpatient settings for most cases. However, rare life-threatening presentations may necessitate intensive inpatient care. While, its precise cause remains elusive, genetic predisposition is evident, and ongoing research investigates the immune system's role. Though potentially autoimmune, the absence of a defined autoantigen adds complexity. Triggers like trauma, sunburn, infections, medications, and stress can provoke psoriasis, contributing to its complex etiology [6].

❖ Epidemiology of psoriasis

Psoriasis exhibits a gender-neutral impact but often manifests earlier in females and individuals with a familial predisposition. The age of onset demonstrates distinct peaks, notably between 30–39 and 60–69 years in men, occurring roughly a decade earlier in women. Globally, psoriasis prevalence varies markedly across regions, being more prevalent in high-income nations and affecting white populations disproportionately. Its prevalence spans from 0.1% in East Asia to 1.5% in Western Europe, while Egypt showcases a prevalence ranging from 0.19% to 3%. The condition's genetic underpinnings are evident in around 30% of affected patients, with identified genes potentially contributing to susceptibility. Moreover, the high concordance observed in monozygotic twins supports the genetic

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basis of psoriasis, although environmental factors and immunological disparities further shape the disease's manifestations and presence [7].

❖ Aetiopathogenesis of psoriasis

Psoriasis development involves immunological cascades centered on adaptive immune pathways like IL-17 and IL-23, with intricate interplay between innate and adaptive systems. Genetic factors, unveiled by genome-wide studies, spotlight over 80 loci contributing to around 30% of disease heritability. HLA-C emerges as a major genetic risk for early-onset psoriasis, while variants impacting innate and adaptive immunity pathways, including IFNs, IL-23, IL-17, and NF-Kβ, play pivotal roles. Psoriasis manifestation hinges on gene-environment interplay. Environmental triggers such as stress, infections like streptococcus, alcohol, drugs, and sunlight alongside obesity can precipitate or result from psoriasis, a process involving complex interactions between genetics and the environment [8].

The pathogenesis of psoriasis underscores the involvement of various immune cells, particularly T cells, dendritic cells, and keratinocytes, communicating via cytokines like TNFα, IFN-γ, IL-17, and IL-22. These interactions induce epidermal changes, angiogenesis, and inflammation, perpetuating the disease cycle. Tissue-resident memory T cells play a crucial role, persisting in the skin and contributing to recurrent psoriasis episodes. Additionally, cytokine networks, including IL-23, IL-17, TNF-α, and IFN-γ, act as key drivers in different phases of psoriasis, influencing plaque formation and immune responses. Their interplay results in complex inflammatory circuits, amplifying each other and contributing to the sustained inflammation characteristic of psoriasis [9].

❖ Clinical types of psoriasis

The clinical spectrum of psoriasis encompasses various forms, with chronic plaque psoriasis standing out as the most prevalent and easily identifiable. Its distinct characteristics include well-defined salmon-pink plaques with silvery scales in lighter skin and greyish plaques in darker skin, often symmetrically distributed across areas like knees, elbows, the lower back, and the scalp. Less common types involve guttate psoriasis, presenting as small scaly papules in a centrifugal pattern, erythrodermic psoriasis, severe and marked by extensive erythema and scaling over large body surface areas and pustular psoriasis, characterized by sterile pustules and erythema. Further classified into generalized, palmoplantar, and acrodermatitis continua of Hallopeau. Inverse psoriasis occurs in skin folds, appearing red and shiny without the usual scales, while nail psoriasis displays multiple variations, from nail pitting and onycholysis to discoloration and nail plate damage, often linked with an increased risk of psoriatic arthritis. Each subtype showcases unique clinical features and presentations, aiding in their identification and differentiation [10].

Pruritus in psoriasis

Pruritus in autoimmune and inflammatory dermatoses, is a common symptom that can be severe and affects patient's quality of life. In some diseases, pruritus is related to disease activity and severity or may occur independently of the disease [11].

❖ Epidemiology of pruritus in psoriasis

Studies have notably shifted the understanding of psoriasis from being non-pruritic to recognizing pruritus as a prevalent symptom, affecting a majority of individuals with the condition. Initially perceived differently, early studies by Newbold (1977) identified pruritus in 92% of hospitalized psoriasis patients, setting a new understanding of its prevalence. Subsequent investigations consistently echoed these findings, establishing pruritus in around 60–90% of psoriasis cases. Of significance, pruritus emerged as the most frequently reported subjective sensation and the most distressing symptom among individuals with psoriasis [12, 13].

❖ Pathogenesis of pruritus in psoriasis

Understanding the complex pathogenesis of pruritus in psoriasis has revealed several intriguing mechanisms. One prevailing concept centers on neurogenic inflammation, wherein the interplay between nerves, skin components, and the immune system contributes significantly to pruritus development. This theory finds support in observations linking emotional stress with the onset and exacerbation of pruritus in psoriasis. Various neuropeptides and receptors, including substance P, calcitonin gene-related peptide, and others exhibit altered expression and secretion in psoriatic skin, with a direct association established between these abnormalities and pruritus. Studies have detected an increased number of substance P-positive nerves in the perivascular area of psoriatic patients with pruritus, highlighting the potential role of these neuropeptides in eliciting itch [14].

Moreover, abnormal innervation patterns and neurotrophic factors like nerve growth factor (NGF) and semaphorin-3A have been implicated in pruritus genesis. Increased expression of NGF, coupled with decreased levels of semaphorin-3A, correlates with heightened nerve fiber density in the epidermis, potentially contributing to pruritus. Distinctly, the dysregulation of the opioid system in psoriatic skin, specifically reduced expression of κ-opioid receptors, has been linked to pruritus. An imbalance favoring μ-opioids over κ-opioids might promote itch, further supported by observations of enhanced pruritus upon μ-opioid receptor activation [15].

Additionally, pruritus may involve vascular abnormalities, as suggested by increased levels of endothelial markers like endothelial leucocyte adhesion

molecule 1 (ELAM-1) and E-selectin in psoriatic patients with pruritus. Elevated serum levels of soluble vascular adhesion protein 1 (VAP-1) were found in these individuals, indicating potential vascular contributions to pruritus. Furthermore, mast cell activation and their proximity to unmyelinated nerve fibers in pruritic skin imply a role for mast cells in mediating itch sensations, a phenomenon not observed in non-pruritic skin [13].

❖ Clinical characteristics of pruritus in psoriasis

Clinical features of pruritus in psoriasis encompass a diverse array of manifestations. While itch often localizes to psoriatic plaques, it frequently extends beyond these regions to involve unaffected skin, sparing the face and neck in most cases. However, some individuals experience generalized pruritus that encompasses the entire body surface. Notably, pruritic sensations and burning may affect the genital area, particularly in women, irrespective of the presence of psoriatic plaques. The severity of pruritus, typically assessed through the visual analogue scale (VAS), commonly falls within the moderate range, indicating significant discomfort for most psoriasis patients. Researchers have noted varying degrees of correlation between pruritus intensity and psoriasis severity, with some studies confirming a significant association, albeit modest, while others have failed to establish a consistent link [16].

The nature of pruritus in psoriasis spans a spectrum of sensations, including stinging, pinching, tickling, crawling, and even pain, often experienced concurrently with itching. Reports suggest that pruritus severity intensifies at night and during winter, with higher prevalence and intensity observed among women compared to men. Factors such as the duration of psoriasis, marital status, and family history of psoriasis or atopy seem to have little influence on pruritus intensity. Pruritus exacerbation is commonly linked to heat, skin dryness, hot water, sweating, and emotional stress, while relief often accompanies improved skin lesions and is associated with factors such as cooler showers and better sleep quality [17].

❖ The effect of pruritus on patients' QoL

Pruritus in psoriasis profoundly impacts patients' quality of life across various dimensions. It's often cited as the most bothersome symptom of the disease, contributing significantly to perceived disease severity. Studies indicate that patients experiencing pruritus report a more substantial decline in health-related quality of life compared to those without this symptom. **Elewski *et al.*** [18] highlighted its negative influence on mood, concentration, sleep, sexual desire, and appetite, illustrating the pervasive effect on multiple aspects of daily life. This symptom also correlates with increased depressive symptoms and feelings of stigmatization among psoriatic individuals, underlining its substantial psychological toll.

Moreover, the severity of pruritus is associated with compromised physical functioning and can significantly impact work ability. Nearly half of the individuals surveyed attributed pruritus as the primary psoriasis symptom hindering their work activity. The coping strategies adopted by patients with pruritus differ from those without, revealing that a stronger fighting spirit corresponds to less severe pruritus in terms of intensity and frequency of episodes. This suggests a complex interplay between psychological disposition and the experience of pruritus, emphasizing the potential benefits of tailored psychological interventions for individuals grappling with severe pruritus in psoriasis [19].

❖ Treatment of pruritus in psoriasis

Treating pruritus in psoriasis often aligns with addressing the resolution of skin lesions, given the relief typically associated with disease remission. While, there isn't a specific targeted therapy solely for psoriatic pruritus, ongoing research suggests potential treatments. Studies like that of **Roblin *et al.*** [20] phase 2b trial on Trk-A inhibition with CT327 showed promise for managing pruritus in psoriasis, potentially offering future therapeutic options pending further confirmation in subsequent studies.

Therapeutic interventions like narrowband UVB therapy have demonstrated efficacy in alleviating psoriatic pruritus, although in some cases, this treatment might exacerbate itching by drying the skin. Antihistamines are generally considered ineffective unless they induce sedation, with more severe cases sometimes requiring oral antidepressants like mirtazapine for relief, particularly in erythrodermic psoriasis. Beyond pharmacological approaches, family and professional support play a crucial role in aiding patients' coping mechanisms against itching, while more resistant cases might explore options such as κ-opioid agonists or GABA-ergic drugs. Additionally, certain biologics like etanercept have shown potential in reducing pruritus intensity, offering another avenue for managing this challenging symptom [21].

Recommendations and future prospectives:

Recommendations and future perspectives in psoriatic pruritus hold immense potential. Further studies are urgently needed to provide clarification of the mechanisms involved in the pruritus in psoriasis to develop better medications for psoriatic itch. Since pruritus is a significant determinant of patients' quality of life, physicians should be aware that even effective anti-psoriatic therapies may not necessarily control pruritus or the occurrence of pruritus in responders to anti-psoriatic treatment may be a fist symptom of growing secondary unresponsiveness.

CONCLUSIONS

Pruritus is a prevalent and distressing symptom in psoriasis, affecting a majority of individuals with the

condition. Understanding these mechanisms could pave the way for targeted therapies addressing pruritus in psoriasis. Treatment of pruritus in patients with psoriasis should be directed towards the resolution of skin lesions, as disease remission usually is linked with pruritus relief.

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