Review Article

A review on updates in management and Treatment of Psoriasis

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Abstract

Introduction: Introduction: Psoriasis is a rather common inflammatory skin disease that is characterized by the appearance of red scaly plaques and may affect any part of the body. There are certain factors that make psoriasis a challenge for physicians, these include: high prevalence, disability, chronicity, disfiguration, and associated comorbidities. The approach to the management of Psoriatic patients should also take into account the dermatological clinical features. This review would discuss and focus on recent updates in the management of Psoriatic patients and its common related issues as well as the clinical picture of psoriasis in order to understand and inform medical practitioners and develop their knowledge of the etiology of the condition, immune and environmental factors, has led to the development of precision-targeted therapies that alleviate patient morbidity. **Methodology:** PubMed database was searched and screened for relevant observational studies, systematic reviews, randomized controlled trials, meta-journal articles, and journal articles containing the term used in the mesh "Psoriasis", "Management" "Treatment trials" within the title or abstract. **Conclusion:** The physician should adhere to updated evidence-based guidelines in the management of psoriatic patients. New biologic modalities and alternative nature-based treatments for psoriasis should be studied. Pharmacodynamics profiles, administration modality, and dosing regimens for the currently available IL-17 and IL-23 inhibitors must be re-examined to improve the overall continuity of care of psoriasis patients.

Keywords: Psoriasis, Diagnosis, Management

Introduction

Psoriasis is a known chronic inflammatory condition of the skin as well as joints and is accompanied by emotional and social complications that lead to significant disabilities with profound impaired quality of life.

Psoriasis is a disease known in medical text from Greek times, and these patients were cast out from societies. The main reason for this was a misconception, as people feared that psoriasis was an infectious disease. In addition to this misconception, medical practitioners of previous eras failed to recognize psoriasis as a non-infectious chronic dermatological disease. [1]

While the etiology still remains unknown to this day, epidemiological studies focused on understanding the pathogenesis contribution revealing predisposing genetic and autoimmune traits in the process of the disease. The ideal goal of treating patients with psoriasis is to optimize the controls of symptoms, improve quality of life, psychological comorbidity, and prevent structural damage and disability. [2, 3]

This review will discuss and focus on recent updates in the approach to the management of Psoriasis and its common related issues as well as the clinical picture of psoriasis in order to understand and inform medical practitioners. Additionally, to guide the physician in lessening patient mortality and morbidity.

Methodology

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PubMed database was searched, relevant observational studies, systematic reviews, randomized controlled trials, meta-journal articles, and journal articles containing the term "Psoriasis", "Management" "Treatment trials" within the title or abstract. The primary search strategy was largely limited to eligible English language publications and that describes outcome measures were conducted. Original articles on the management, diagnosis, and approach to the clinical situation of the patient were included.

Review

Psoriasis is a prevalent chronic inflammatory disease that affects the skin, nails, and joints and has a strong genetic predisposition and autoimmune pathogenic traits affecting approximately 2–4% of males and females in western countries but varies depending on the region. [4] Psoriasis tends to persist lifelong, fluctuating in severity and extent. The prevalence of this condition is higher in the adult population almost four times more than the pediatric population. It has a bimodal incidence in young adulthood and another in late adult life at 60 years of age. It can start at any age including a childhood in approximately one-third of the cases, with peaks of onset at 15–25 years and 50–60 years.[5, 6] As for adult psoriasis, with peaks in age classes characteristic of early-onset (35-44 years) in late-onset psoriasis (65-74 years) revealed some variations according to gender, i.e. females are diagnosed earlier than males suggesting a higher mortality rate in the elder population.[7, 8] Psoriasis in children has a higher prevalence in being associated with juvenile arthritis, obesity, increased waist circumference percentiles and waist-to-height ratios, metabolic laboratory abnormalities, and psychiatric disorders.[6, 9, 11] It is particularly common in Caucasians but may affect people of any race. Prevalence in Europe varies from 0.73% to 2.9%, similar to the Unites States (0.7%–2.6%) and higher than Latin America. However, it shows a lower prevalence in Asia and Africa (from 0 to <0.5%). [12, 13]

The pathophysiology of psoriasis is not completely understood. However, multiple theories postulate that there is a primary role of immune reactions and is characterized by epidermal hyperproliferation, enhanced antigen presentation, Th-1 cytokine production, and T-cell expansion. There is often a genetic predisposition following a complex polygenic inheritance.

It has long been argued that genetic involvement may be the key to understanding the development of the psoriatic disease. Genetic investigations have shown that a specific gene plays a central role in the causation of this condition. This gene is known as PSORS-1 and is considered of high specificity as its identification almost confirms the presence of psoriasis.[14] Literature suggests that almost half of patients with psoriasis have at least a first-degree with the disease.[15]

In almost half of the psoriatic patients, the disease occurs in a rather inherited pattern. Studies have suggested that particular human leukocyte antigen HLA traits are associated with the development of the condition. Furthermore, the affected psoriatic patients usually start displaying symptoms in their twenties to thirties. This type of psoriatic illness is termed type-1 psoriasis. Another HLA variant presents in the overwhelming majority of patients who suffer from psoriatic disease before the fifth decade of age, typically present with more severe manifestations. [16, 17]

Environmental factors also trigger an exacerbation, including trauma (Kobner phenomenon), infections caused by streptococcal, staphylococcal, human immunodeficiency virus which often worsen psoriasis, or precipitates explosive forms as well as alcohol and drugs (eg. antimalarial, botulinum A, beta-blockers, lithium, Iodides, aspirin, withdrawal, and steroid). Moreover, stressful life events and emotional upset seem to cause some exacerbations. Sunlight improves most psoriatic but 10% become worse. [16, 17]

Findings on physical examination are varied depending on the type of psoriasis and dermatological manifestations of psoriasis. The most prevalent skin manifestations include plaques, papules, erythematous/salmon-colored macules, and scaling. Psoriasis vulgaris is the most prevalent type in around 90% of cases. Classical clinical manifestations in psoriasis vulgaris are sharply demarcated raised lesions covered in silvery scales. This is most common on the extensor surfaces of the limbs and the scalp. [18] However, inverse psoriasis affects intertriginous locations also known as flexural psoriasis, its characterized by smooth, inflamed lesions without scaling due to the moist nature of the area where this type of psoriasis is located. [19]

Moreover, Guttate psoriasis is a particular form of psoriasis with widespread, small erythematosquamous salmon-pink papules, 1-10 mm in diameter, predominately on the trunk; the lesions may be scaly. The eruption guttate psoriasis is often triggered by group A streptococcal infection that appears frequently 2-3 weeks after an upper respiratory infection. About a third of guttate psoriasis-affected individuals would progress to plaque psoriasis.[20] Furthermore, Pustular psoriasis is a rare form and has serious life-threatening complications including skeletal and joint disease seen in the generalized type of pustular psoriasis. There are salient systemic manifestations of the generalized form of pustular psoriasis, including fever, pain, and malaise.[21] However, acrodermatitis continua of Hallopeau and palmoplantar pustulosis are localized and are characterized by limited disease of the feet and hands. On the other hand, acrodermatitis continua is more distally located at the tips of the toes and fingers and affects the nail apparatus. When pustular forms of the disease present in the latter manner, a dermatologic biopsy would be indicated to confirm the disease. [22]

Erythrodermic psoriasis is considered an acute condition in which >90% of the body is covered with inflamed surfaces and is considered a skin marker of HIV infection when occurs in recalcitrant psoriasis or in previously healthy patients.[23, 24]

Involvement of the nails is common and affects 80%-90% of patients with plaque psoriasis, with "Pitting", onycholysis, and sometimes subungual hyperkeratosis. It is even more common in patients with psoriatic arthritis.

The diagnosis of many differentials of psoriasis, including rheumatoid arthritis and gout, is clinically based. Therefore, differentiating between these autoimmune conditions relies on the presence or lack of typical laboratory features of each diagnosis. [25]

Psoriatic arthritis (PsA) systematic review revealed a fifth of these patients are suffering from mild to severe arthritis with psoriasis, which is characterized by enthesitis. Additionally, arthritis would present with peripheral as well as axial involvement, combined at the physiopathological level with bone proliferation and erosion.

The pathophysiology of psoriatic arthritis begins with the activation of innate immune cells in the enthesitis phase of the condition. Afterward, when specific entheseal cells are stimulated with IL-23, they secrete inflammatory cytokines such as TNF-α, IL-22, and IL-17A, thus augment inflammation. Asymmetric involvement of joints is present in psoriatic arthritis, characteristically these patients would present with unilateral distal interphalangeal joint inflammation. [26]

In addition to skin manifestations, ocular manifestations are relatively common and mainly include blepharitis conditions. This latter condition presents as edematous erythematous psoriatic plaques that result in madarosis, cicatricial ectropion, trichiasis, and even loss of the lid tissue. Psoriatic plaque in ocular manifestations can extend from the lid to the conjunctiva. Corneal disease is relatively rare and it is most often secondary to the lid or conjunctival complications. It is recommended that regardless of risk factors, psoriatic patients should undergo regular eye exams in order to monitor for the progression of asymptomatic or symptomatic ocular manifestations. [27]

The diagnosis of psoriasis is primarily clinical and the severity of the disease can aid in the management of psoriasis. Early evaluation and identifying differential diagnosis of psoriasis increase diagnostic accuracy and the therapy of choice. The clinical categorization of the psoriatic disease depends on the clinical severity of the lesions, as patients could be grouped into either severe, moderate, or mild psoriatic disease. Moreover, other factors are important in the former categorization format and include: affected body surface area with skin lesions along with the quality of life. The PASI score has been extensively used in clinical trials as severity and response to treatment are important clinically, as they guide the physician in appropriate treatment approach and effectiveness or adverse effect of chosen treatment modality. A PASI of ≥10 or a DLQI of ≥10 indicates severe disease. [28]

Topical glucocorticoids along with vitamin D and phototherapy could be used to manage psoriasis disease, provided that it is not severely manifested. Moreover, severe psoriasis would not be properly managed by topical therapy alone and would require systemic medication. In patients with psoriatic arthritis, the physician should attempt to discuss treatment options carefully as these patients could be non-compliant due to their disability.[2] Furthermore, an alternative to insufficient symptomatic relief is phototherapy and systemic therapies such as small-molecule (traditional and new) and biologic drugs are recommended during severe stages of psoriasis. [29]

The approach to psoriatic treatment depends on the extent of the disease, its progression, and its effect on daily living. In this manner, the physician could discuss treatment options with the patient to set realistic outcomes on symptomatic control. Around 60% of patients suffering from mild manifestations of psoriasis could achieve satisfactory treatment results by topical therapy alone. Unfortunately, the lack of practical guidance by physicians who prescribe those topical therapies renders it difficult for patients to comply with the management plan. The role of specialist nurses has gained more importance with the help and advice of the application of topical therapy that has greatly improved clinical outcomes.

Among the oldest therapies used to manage psoriasis are crude coal tar and dithranol. These methods are used under a doctor's supervision usually as a part of the day-clinic. This is done because of the difficulties associated with their application. Particular body locations (e.g., scalp, flexures, and face) are difficult to treat. The rising risk of skin atrophy and perioral dermatitis has rendered the role of steroids in the management of psoriasis obsolete.

Biologic agents demonstrated tolerable safety profiles in the clinical trials as no guidelines exist for the biologic switch in psoriasis after treatment failure. However, high rates of complete clearance of psoriasis have been reported with biologics that target interleukin 17 (IL-17) or IL-23. Long-term maintenance of the clinical response is observed with the following biologics: secukinumab, ixekizumab, guselkumab, and risankizumab.

Out of all these medications, Brodalumab is the only medication with early efficacy onset, approximately, half of the efficacy is reached within 2 weeks. Other immunomodulators (e.g. ixekizumab) are usually required to complete this effect. [30] Table 1 summarises newer drugs that are available for psoriasis therapy.

Table 1: Drugs available for psoriasis therapy.[30]

Drug	Mechanism	Application
Methotrexate	Dihydrofolate reductase inhibition blocks purine biosynthesis; induction of lymphocyte apoptosis	s.c./oral
Cyclosporin	Calcineurin inhibition leading to reduced IL-2	Oral
Acitretin	Normalization of keratinocyte proliferation/differentiation through retinoid receptor binding	Oral
Fumarate	Intracellular glutathione, modulation of Nrf2, NF-κB, and HIF-1α; promoting a shift from a pro-inflammatory Th1/Th17 response to an anti-inflammatory/regulatory Th2 response.	Oral
Apremilast	PDE4 inhibitor increases intracellular cAMP levels in immune and non-immune cells modulating inflammation	Oral
Etanercept	Dimeric human fusion protein mimicking TNF-αR	s.c.
Infliximab	Chimeric monoclonal IgG1κ antibody that binds to soluble and transmembrane forms of TNF-α	i.v.
Adalimumab	Human monoclonal antibody against TNF-α	s.c.
Certolizumab	Fab portion of human monoclonal antibody against TNF-α conjugated to polyethylene glycol	s.c.
Ustekinumab	Human monoclonal IgG1k antibody that binds with specificity to the p40 protein subunit used by both IL-12 and IL-23 cytokines IL-12/IL-23 p40	s.c.
Tildrakizumab	Humanized IgG1κ, which selectively blocks IL-23 by binding to its p19 subunit	s.c.
Guselkumab	Human monoclonal IgG1λ antibody that selectively blocks IL-23 by binding to its p19 subunit	s.c.
Risankizumab	Humanized monoclonal IgG1 antibody, which inhibits IL-23 by specifically targeting the p19 subunit	s.c.
Secukinumab	Human monoclonal IgG1κ antibody against IL-17A	s.c.
Ixekizumab	Humanized, monoclonal IG4κ antibody selectively binds and neutralizes IL-17A	s.c.
Brodalumab	Human monoclonal IgG2 antibody directed at the IL-17RA	s.c.

Recent studies stated that Ustekinumab and secukinumab are associated with the highest and lowest drug survival, respectively, although most patients on secukinumab were non-naïve. Secukinumab had the most frequent rate of adverse effects in patients with psoriasis. [31] New biologics such as IL-23 or IL-17 antagonists show greater responses in bio-experienced patients and could even be utilized for patients in previous failed treatments.[32] Biologics targeting interleukin (IL)-17 and IL-23 are generally well-tolerated and considered safe, though adverse events are seen more often compared with placebo. Pharmacological studies have found that novel modalities using interleukins 17 and 23 inhibitors were tolerated in patients with psoriasis, with mild sild effects. [33]

Nevertheless, recent evidence has reported a subpar pharmacological effect of these agents. However, more evidence is still required to make a final judgment. Other recent studies have reported that treatment methods using tumor necrosis factor-alpha inhibitors were associated with a dramatic increment in infection rates. Other adverse effects of these immunomodulators include susceptibility to tuberculosis, lupus, and other immune or infusion reactions. Side effects such as candidiasis and decremented leucocytes were associated with IL-17 inhibitor usage. Currently, no literature has reported any specific adverse effects related to interleukin-23 inhibitors. [34]

Reconsidering climatotherapy for a safe and efficient replacement to the standard management modalities. Climatotherapy comprises alternative treatment methods such as thalassotherapy, where these methods are based on the healing capacities of natural resources. [35]

Conclusion

Psoriasis remains a prevalent disease in the dermatological community, but is still considered under-diagnosed and not properly managed due to many factors. This signifies the importance of a multidisciplinary approach to the treatment of the condition along with any autoimmune diseases that co-exist. A better understanding of new biologic modalities alternative nature-based treatments for psoriasis should be studied as well as dosing regimens, administration modality, and pharmacodynamics profiles for the currently available IL-23 and IL-17 inhibitor may require essential appraisal as they are central for a proper approach to management and quality of life in these patients.

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