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A COMPREHENSIVE REVIEW ON THE THERAPEUTIC ROLE OF CORTICOSTEROIDS IN DERMATOLOGICAL DISEASE MANAGEMENT

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ABSTRACT

Skin diseases represent a significant global health burden, affecting millions of individuals and contributing substantially to morbidity and reduced quality of life. Common dermatological conditions such as psoriasis, atopic dermatitis, seborrheic dermatitis, contact dermatitis, acne vulgaris, and vitiligo are largely driven by inflammatory and immune-mediated mechanisms. Among available therapeutic options, corticosteroids remain a cornerstone in dermatological practice due to their potent anti-inflammatory and immunosuppressive properties. This review provides a comprehensive overview of the role of corticosteroids in the management of various skin disorders, focusing on their mechanisms of action, clinical applications, pharmacokinetics, pharmacodynamics, and classification. It also highlights appropriate prescribing practices, including selection of potency, duration of therapy, and methods to enhance patient adherence while minimizing adverse effects. Special emphasis is placed on safety concerns associated with prolonged or inappropriate use, such as local skin changes and systemic complications. This review aims to provide a comprehensive overview of the therapeutic effectiveness, clinical applications, safety considerations in corticosteroid therapy for dermatological conditions.

KEYWORDS: Topical corticosteroids, Skin diseases, Dermatology, Inflammation, Psoriasis and Atopic dermatitis.

INTRODUCTION

Skin diseases are among the most prevalent health conditions globally and contribute significantly to overall morbidity across diverse populations. These disorders include a wide range of conditions such as inflammatory, allergic, autoimmune, and infectious diseases that compromise both the structure and physiological function of the skin. Frequently encountered conditions like atopic dermatitis, psoriasis, contact dermatitis, and various forms of eczema are commonly associated with chronic inflammation, intense itching, redness, and impairment of the skin's protective barrier[1,6] From a global perspective, dermatological disorders represent a substantial non-fatal disease burden. Data reported by international organizations, including the World Health Organization, consistently demonstrate that skin conditions are one of the leading causes of disability worldwide. Large epidemiological studies, such as those conducted under the Global Burden of Disease initiative, indicate that hundreds of millions of individuals are affected by skin diseases at any given time, making them one of the primary reasons for seeking outpatient medical care. In India, skin disorders also account for a notable proportion of healthcare utilization. Evidence from both institutional and community-level studies suggests that approximately 6–10% of outpatient visits are attributed to dermatological complaints.[9]

The distribution and frequency of these conditions are influenced by various environmental and demographic factors, including tropical climate, elevated humidity, occupational hazards, hygiene practices, and genetic susceptibility. Inflammatory skin conditions are particularly common; psoriasis affects an estimated 0.4–2.8% of the population, while eczema and other dermatitis conditions show variability depending on age,

region, and lifestyle factors. In addition to their physical symptoms, chronic dermatological conditions can have a profound impact on psychological and social well-being. Persistent itching, visible lesions, and recurrent disease episodes often lead to emotional distress, reduced confidence, social withdrawal, and a diminished quality of life.[7,9] These factors highlight the importance of effective and patient-centered treatment strategies. Corticosteroids have remained a fundamental component in the treatment of inflammatory skin diseases for several decades. Their therapeutic efficacy is primarily due to their ability to suppress inflammatory pathways, reduce immune system activity, and decrease capillary permeability in affected tissues.[10] This review aims to provide a comprehensive overview of the therapeutic effectiveness, clinical applications, safety considerations in corticosteroid therapy for dermatological conditions.

Skin and inflammation

The skin is the largest and one of the most functionally complex organs of the human body, acting as a crucial boundary between the internal physiological environment and the outside world. In adults, it typically covers an area of approximately 1.8 to 2.0 square meters and plays a central role in preserving internal balance. Although it is widely recognized for its role as a physical barrier against environmental threats such as microorganisms, chemicals, and ultraviolet radiation, the skin also serves as an active immunological organ. It possesses the ability to sense external stimuli and initiate appropriate biological responses to maintain tissue integrity and protect the body from harm.[11] Embedded within the skin is a highly organized immune system that continuously monitors for potential threats. This system operates through two major arms: innate immunity and adaptive immunity, both of which function together to provide effective defense. Innate immunity represents the immediate response mechanism and is non-specific in nature. It involves a range of immune cells, including neutrophils, macrophages, mast cells, eosinophils, basophils, dendritic cells, and natural killer cells. Specialized antigen-presenting cells, such as Langerhans cells located in the epidermis and dendritic cells in the dermis, play a pivotal role in identifying foreign substances and initiating immune reactions. These immune cells detect invading pathogens or tissue injury through pattern recognition receptors, which identify common molecular patterns associated with microbes or damaged cells. Once these receptors are activated, a cascade of defense mechanisms is triggered. This includes the release of cytokines and other inflammatory mediators, activation of complement systems, enhancement of phagocytic activity, and recruitment of additional immune cells to the affected site. This rapid response not only limits the spread of pathogens but also facilitates the activation of more specialized immune processes. Adaptive immunity, in contrast, provides a highly specific and targeted defense against particular antigens. This system is primarily mediated by T lymphocytes and B lymphocytes. T cells regulate immune responses by producing cytokines and directly destroying infected or abnormal cells, while B cells are responsible for the production of antibodies that neutralize pathogens and assist in their removal.[12,13]

A key advantage of adaptive immunity is its ability to develop immunological memory, which ensures a faster and more efficient response upon repeated exposure to the same antigen. The coordination between innate and adaptive immune systems is essential for maintaining a balance between effective defense and tissue preservation. Under normal circumstances, immune responses are tightly regulated to prevent unnecessary inflammation and damage to healthy cells. However, when this regulation is disrupted, the immune system may become overactive or misdirected. Such dysregulation can lead to the development of autoimmune and inflammatory conditions, where the body's own tissues are targeted or subjected to prolonged inflammation. Several skin disorders arise from these abnormal immune responses. Conditions such as psoriasis and atopic dermatitis are characterized by chronic inflammation driven by immune system dysfunction. The development of these diseases is influenced by multiple factors, including genetic predisposition, hormonal changes, environmental exposures, and interactions with microorganisms. External triggers such as infections, ultraviolet radiation, chemical irritants, and psychological stress can further aggravate these conditions in susceptible individuals. Persistent activation of immune pathways and excessive production of inflammatory mediators can result in long-term damage to skin tissues. This may lead to structural alterations, impaired barrier function, and visible clinical manifestations.[11,15]

Psoriasis

Psoriasis is a persistent inflammatory disorder of the skin driven by immune system dysregulation, resulting in rapid turnover and faulty maturation of epidermal cells. The term originates from a Greek word meaning "itch," reflecting a frequent symptom experienced by patients. The condition develops due to a multifaceted interaction between inherited susceptibility, altered immune responses, and external environmental influences. Although psoriasis may arise at any age, it most commonly begins in early adulthood, with another increase in incidence observed in middle age. The disease affects individuals of all genders equally and is not transmissible through physical contact. Epidemiological patterns of psoriasis differ across regions of the world.[16,19] On a global scale, the condition is estimated to affect approximately 1–3% of the population, though certain regions report higher figures. For instance, populations in Northern Europe show relatively elevated prevalence rates, whereas lower rates are documented in many Asian and tropical countries. In India, psoriasis is a commonly encountered dermatological condition, affecting roughly 0.4% to 2.8% of the population. These variations may be

influenced by climatic conditions, genetic diversity, environmental exposures, and lifestyle-related factors. At the biological level, psoriasis is characterized by an exaggerated immune response within the skin. Immune cells, including T lymphocytes, dendritic cells, and macrophages, become activated and release inflammatory mediators such as tumor necrosis factor-alpha, interleukin-17, and interleukin-23. These signaling molecules promote excessive proliferation of keratinocytes and interfere with their normal differentiation process, leading to thickened, scaly skin lesions.[20] Clinically, psoriasis is typically recognized by well-defined, erythematous plaques covered with silvery scales. These lesions commonly occur on the scalp, elbows, knees, and lower back. Patients may experience symptoms such as itching, irritation, and a burning sensation, which can significantly impact daily activities. In addition to skin involvement, approximately one-quarter of patients may develop Psoriatic Arthritis, a condition that affects the joints and may lead to long-term disability if not properly managed.[21]

Treatment strategies are guided by disease severity and the extent of body surface involvement. In mild cases, topical therapy is generally sufficient. Corticosteroids remain one of the most frequently prescribed topical agents due to their strong anti-inflammatory and immunosuppressive actions. They help reduce redness, scaling, and itching by suppressing inflammatory pathways and limiting immune cell activity in affected areas. These medications are available in different potency levels and are often used alongside other topical agents, such as vitamin D analogues, to enhance treatment outcomes. For individuals with moderate to severe disease, additional therapeutic approaches are required. These may include phototherapy, systemic medications such as methotrexate and cyclosporine, and targeted biologic therapies that inhibit specific inflammatory cytokines.[22,23]

Atopic Dermatitis

Atopic Dermatitis is a persistent inflammatory skin condition marked by recurrent episodes of dryness, intense itching, and eczematous lesions. It is the most frequently encountered form of eczema and typically begins during infancy or early childhood, although symptoms may continue or re-emerge later in life. The name reflects its pathological nature, combining terms that denote skin involvement and inflammation. The pattern of disease presentation varies according to age.[24] In infants, lesions commonly appear on the cheeks and outer surfaces of the limbs. As individuals grow older, the distribution tends to shift toward flexural regions, including the inner aspects of the elbows and knees, as well as the neck. A key clinical feature is persistent itching, which often leads to repeated scratching. This cycle of itching and scratching can worsen skin damage, increase susceptibility to infection, and interfere with sleep, ultimately affecting daily functioning and overall well-being. The frequency of atopic dermatitis differs significantly across populations and regions. Higher rates are generally observed in industrialized countries, particularly in parts of Europe and Australasia, whereas lower prevalence is noted in certain Asian and Eastern European regions. In the United States, the condition affects a considerable proportion of children, with estimates ranging from about 8% to 18%. In India, studies indicate that approximately 2% to 10% of children are affected, although this varies depending on environmental conditions, geographic location, and socioeconomic status.[24,26]

Factors such as urban development, pollution, and lifestyle changes are thought to contribute to the increasing incidence of the disease. The development of atopic dermatitis involves multiple interacting factors. One of the primary contributors is a defect in the skin barrier, which leads to increased water loss and allows allergens and microorganisms to penetrate more easily. Genetic variations affecting proteins responsible for maintaining skin integrity play an important role in susceptibility. In addition, immune system alterations are central to disease progression. There is an enhanced immunoglobulin E–mediated response along with activation of T-helper cell pathways, which results in the release of inflammatory cytokines that sustain chronic inflammation and itching. Although a permanent cure is not currently available, effective management can significantly reduce symptoms and improve quality of life.[27]

Treatment strategies focus on controlling inflammation, relieving itching, and restoring the skin barrier. Topical therapy forms a fundamental component in the management of eczema and is widely used to control inflammation and alleviate symptoms. A variety of topical agents are available, including topical corticosteroids, calcineurin inhibitors, phosphodiesterase-4 inhibitors, Janus kinase inhibitors, medicated emollients, and several newer investigational treatments under development. Among these options, topical corticosteroids remain the most commonly prescribed due to their strong anti-inflammatory effects. Clinical evidence suggests that corticosteroids with moderate to high potency are generally more effective in promoting lesion resolution compared to those with low potency. However, no significant difference in therapeutic outcomes has been consistently observed between intermediate- and high-potency formulations.[28] Regarding frequency of application, once-daily use of topical corticosteroids has been found to provide similar benefits to twice-daily regimens, which may improve patient adherence and reduce potential adverse effects. In addition, proactive treatment strategies, such as applying topical corticosteroids intermittently (for example, on two consecutive days each week), have been shown to reduce the likelihood of disease relapse. Regular use of moisturizers and emollients is essential to maintain hydration and reduce flare-ups. Avoidance of known triggers, such as harsh cleansing agents, irritant fabrics, and environmental allergens, is also a key component of management. Topical corticosteroids are considered the cornerstone of therapy for mild to moderate cases due to their strong anti-inflammatory and immunosuppressive effects. They help reduce redness, swelling, and itching by inhibiting inflammatory pathways and decreasing immune activity in affected areas. These agents are available in different strengths and are selected based on disease severity, location, and patient-specific factors, typically for short-term or intermittent use to minimize adverse effects. For patients with more severe or treatment-resistant disease, additional therapeutic options may be necessary. These include topical calcineurin inhibitors, phototherapy, systemic immunosuppressive medications, and biologic therapies that specifically target immune pathways involved in disease progression.[29,30]

Seborrheic dermatitis

Seborrheic Dermatitis is a frequently encountered dermatological disorder that develops in areas rich in sebaceous glands and is closely associated with alterations in the skin's microbial environment. The skin naturally harbors a wide range of microorganisms, including bacteria, fungi, and viruses, which together form the skin microbiota. Among these, lipophilic yeasts of the Malassezia genus are considered key contributors to the development of seborrheic dermatitis under certain conditions. This condition is typically characterized by erythematous, flaky, and sometimes greasy lesions accompanied by itching. The scalp is the most commonly affected site, where it may present as dandruff or more pronounced scaling. Other frequently involved areas include the face (particularly around the nose, eyebrows, and eyelids), upper chest, and skin folds.[31,32] The lesions often appear in a symmetrical distribution and may vary

in severity from mild scaling to more extensive inflammatory involvement. Seborrheic dermatitis affects approximately 1–3% of the general population, although significantly higher rates are observed in individuals with compromised immune function. It is also more commonly seen in patients with certain neurological disorders, including Parkinson's disease. Environmental factors such as low temperature, dry climate, and psychological stress are known to aggravate the condition. Additionally, hormonal influences and increased sebum production are believed to play a role in disease expression.[33]

The underlying mechanism involves an inflammatory response to Malassezia species in susceptible individuals. These organisms utilize lipids present in sebum for growth, producing metabolic by-products that may disrupt the skin barrier and trigger immune activation. This leads to the release of inflammatory mediators, resulting in redness, scaling, and pruritus. Genetic predisposition and immune system variability further influence disease development and severity.[34,36] Diagnosis is primarily based on clinical observation, including the appearance and distribution of lesions. It is important to distinguish seborrheic dermatitis from other skin conditions such as psoriasis, atopic dermatitis, fungal infections, and rosacea, as they may present with similar features but require different management approaches. Treatment focuses on reducing inflammation, controlling microbial growth, and relieving symptoms. Topical antifungal agents, such as ketoconazole and ciclopirox, are commonly used to target Malassezia species. Medicated shampoos and keratolytic agents can help remove scales and improve scalp involvement. For inflammatory symptoms, short-term use of topical corticosteroids is effective in reducing redness and itching. In sensitive areas, topical calcineurin inhibitors may be preferred due to a lower risk of adverse effects with prolonged use. Seborrheic dermatitis often follows a chronic, relapsing course, requiring ongoing management rather than complete cure.[37,38]

Contact Dermatitis

Contact Dermatitis is a frequently encountered dermatological condition that develops following direct exposure of the skin to harmful external substances. It is widely regarded as the most common occupational skin disorder due to repeated contact with irritants and sensitizers in the workplace. In addition to occupational exposure, modern lifestyle practices particularly the increased use of cosmetics, skincare products, and multi-step beauty routines have contributed to a higher incidence of this condition. Frequent application of such products may compromise the skin barrier and alter the normal microbial balance, thereby facilitating the entry of allergens.[39] Contact dermatitis is broadly divided into two types: allergic contact dermatitis (ACD) and irritant contact dermatitis (ICD). ACD is an immune-mediated reaction that occurs in sensitized individuals, whereas ICD results from direct chemical or physical damage to the skin without prior immune sensitization. The diagnosis of allergic forms is primarily confirmed through patch testing, which helps identify the specific causative agent. However, a thorough patient history and clinical examination remain essential for recognizing potential hidden exposures, including those arising from daily habits such as frequent washing, sweating, or contact with personal items. Individuals with Atopic Dermatitis are more vulnerable to developing contact dermatitis due to their compromised epidermal barrier and altered immune responses.[40] Repeated exposure to topical products, even those intended for sensitive skin, may increase the risk of sensitization. Ingredients such as fragrances, preservatives, lanolin, and certain solvents can act as allergens, even when present in products labeled as mild or hypoallergenic.

The pathogenesis of allergic contact dermatitis involves a two-step immunological process. During the initial sensitization phase, small chemical substances penetrate the skin and are captured by antigen-presenting cells, which activate T lymphocytes. Upon subsequent exposure, these primed T cells initiate an inflammatory reaction, typically manifesting within 48 to 72 hours.[41] This response is categorized as a delayed-type hypersensitivity reaction. In contrast, irritant contact dermatitis develops due to direct injury to skin cells, leading to the release of inflammatory mediators and activation of innate immune pathways. Clinically, both types of contact dermatitis may present with itching, redness, and inflammation. Acute cases often show swelling, vesicle formation, and oozing, particularly in allergic reactions. Chronic exposure may result in thickened, dry, and hyperpigmented skin with less clearly defined borders. The pattern of distribution often reflects the site of exposure, with common presentations including hand eczema, eyelid dermatitis, and localized facial or neck involvement. A wide variety of substances can trigger contact dermatitis. Metals such as nickel are among the most frequently implicated allergens, commonly found in jewelry, electronic devices, and clothing accessories. Preservatives and fragrances used in personal care products are also significant contributors. Additionally, certain components in topical medications may act as sensitizers, especially with prolonged use.[42,43]

The cornerstone of management is the identification and avoidance of the causative substance. Educating patients about potential allergens and encouraging careful selection of products are essential for preventing recurrence. Pharmacological treatment focuses on controlling inflammation and relieving symptoms. Topical corticosteroids are typically used as first-line therapy, while topical calcineurin inhibitors may be preferred for delicate areas such as the face. In more severe cases, short-term systemic corticosteroids may be required to achieve symptom control.[44]

Acne vulgaris

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit and is among the most common dermatological conditions worldwide, particularly affecting adolescents and young adults, although it may occur at any age. The condition develops through a complex interplay of factors including increased sebum production stimulated by androgens, abnormal follicular keratinization leading to comedone formation, colonization by Cutibacterium acnes, and subsequent inflammatory responses mediated by immune mechanisms.[45] Clinically, acne presents in both non-inflammatory forms such as open and closed comedones, and inflammatory lesions including papules, pustules, nodules, and cysts, with severity ranging from mild to severe and potentially leading to permanent scarring. Various internal and external factors such as hormonal fluctuations, high glycemic index diets, dairy consumption, stress, environmental conditions, and certain medications like corticosteroids and lithium can aggravate the condition.[46]

The pathophysiology also involves hormonal regulators such as insulin and insulin-like growth factor-1, which enhance sebaceous gland activity and keratinocyte proliferation, thereby worsening lesion formation.[47] Diagnosis is primarily clinical, though hormonal evaluation may be necessary in selected cases, particularly in women presenting with features of hyperandrogenism.[48] Acne not only affects physical

appearance but also has significant psychological consequences, including reduced self-esteem, anxiety, and depression. Management strategies depend on disease severity and include topical agents such as retinoids and benzoyl peroxide, systemic therapies like antibiotics and isotretinoin, hormonal treatments, and procedural interventions including laser therapy and chemical peels.[49]

Vitiligo

Vitiligo is a persistent acquired disorder of pigmentation in which distinct areas of the skin lose their natural color due to the destruction or inactivity of melanocytes. It affects roughly 0.5% to 2% of the global population and occurs with similar frequency in both men and women. Although it does not usually cause physical impairment, the condition can have a major psychological impact, often leading to emotional distress, reduced confidence, and social difficulties.[50] The development of vitiligo is influenced by multiple factors. The convergence theory, which is widely accepted, explains that genetic vulnerability, immune system abnormalities, environmental exposures, and oxidative stress interact to damage melanocytes. In particular, the accumulation of reactive oxygen species and the activation of cytotoxic immune cells are considered central to disease progression. Treatment approaches are selected based on the severity, extent, and activity of the disease. The main objectives are to prevent further depigmentation and to restore skin color. Topical corticosteroids are commonly used because they suppress inflammation and immune responses. Calcineurin inhibitors, such as tacrolimus and pimecrolimus, are also effective in reducing T-cell activity. Additionally, vitamin D analogues contribute to melanocyte growth and function. Among therapeutic procedures, narrowband ultraviolet B therapy is widely preferred due to its effectiveness and improved safety compared to older phototherapy methods. In more severe or rapidly progressing cases, systemic treatments such as oral corticosteroids, methotrexate, cyclosporine, and mycophenolate mofetil are used to regulate immune activity.[51,52]

Recent progress in understanding the molecular mechanisms of vitiligo has led to the development of targeted therapies. Janus kinase inhibitors have shown promising results by blocking key signaling pathways involved in inflammation and melanocyte destruction. Medications like tofacitinib and ruxolitinib are particularly effective when combined with phototherapy.[53] Other emerging therapies include afamelanotide, which enhances pigment production through receptor activation, and peptide-based treatments that stimulate melanocyte regeneration. Furthermore, research is exploring additional targets such as the IL-23/Th17 pathway, immune checkpoint regulators including PD-1 and CTLA-4, and the mTOR pathway, although outcomes differ among patients. Adjunctive therapies, including statins and natural agents like curcumin, may provide additional benefits through their antioxidant and anti-inflammatory properties.[54]

Corticosteroids

Corticosteroids constitute a class of steroid hormones produced by the adrenal cortex and regulated through the hypothalamic–pituitary–adrenal axis. Their release is initiated by adrenocorticotropic hormone from the pituitary gland, which is controlled by corticotropin-releasing hormone secreted from the hypothalamus. These hormones are essential for maintaining internal physiological stability and play a key role in the body's response to stress.[55] The two principal corticosteroids are cortisol, a glucocorticoid, and aldosterone, a mineralocorticoid. Aldosterone primarily governs fluid and electrolyte homeostasis by regulating sodium retention and water balance, while cortisol exerts significant effects on immune and inflammatory processes by inhibiting the release of pro-inflammatory mediators. The therapeutic potential of corticosteroids became evident in the mid-twentieth century when elevated cortisol levels were observed in patients with features of Cushing's syndrome. This observation contributed to the understanding of their anti-inflammatory properties, which were subsequently demonstrated in clinical settings, particularly in individuals with inflammatory conditions such as rheumatoid arthritis[56,57] Over time, extensive research has established that even normal physiological levels of corticosteroids can modulate immune responses and inflammatory pathways, making them valuable agents in medical treatment. In dermatology, corticosteroids are among the most frequently used medications due to their effectiveness in controlling inflammation and suppressing immune activity. In the Indian context, these drugs are widely employed for the management of various skin disorders, including eczema, psoriasis, contact dermatitis, and hypersensitivity reactions. Their

widespread availability, including access without strict prescription regulation, has contributed to both appropriate use and considerable misuse, especially at the community level. Observational data from clinical practice indicate that a significant proportion of patients with chronic dermatological conditions, particularly psoriasis, receive topical corticosteroid therapy either alone or in combination with other agents. However, prolonged and unsupervised use has raised important safety concerns. Commonly reported adverse effects include skin atrophy, steroid-induced acne, rosacea-like eruptions, telangiectasia, and dependence on topical steroids. An additional concern in India is the extensive use of irrational fixed-dose combination products containing corticosteroids along with antifungal and antibacterial agents.[62,63]

Historical Development of Corticosteroid Therapy in Dermatology

The use of corticosteroids in the treatment of inflammatory skin diseases began in the mid-twentieth century with the introduction of systemic corticosteroids, followed soon after by the development of topical formulations. This advancement significantly transformed the management of dermatological conditions, allowing clinicians to effectively control inflammation and immune-mediated skin disorders. Over time, corticosteroids became widely utilized across multiple medical specialties for a broad range of conditions, including skin diseases, respiratory disorders, autoimmune conditions, and rheumatologic illnesses. These agents can be administered through various routes such as oral, topical, inhalational, injectable, and intralesional, reflecting their versatility in clinical practice. Topical corticosteroids were initially considered a safer alternative to systemic therapy, as they were intended to act locally with minimal systemic exposure.[58-59] However, later evidence demonstrated that these drugs can penetrate the skin barrier and enter systemic circulation. The degree of absorption varies depending on several factors, including the patient's age, the site of application, the potency and quantity of the drug, the formulation used, frequency of application, use of occlusion, and the integrity of the skin. In conditions where the skin barrier is compromised, absorption may be significantly increased. With growing clinical experience, concerns have emerged regarding the potential adverse effects associated with prolonged or inappropriate use of topical corticosteroids. These include both local effects, such as skin thinning and telangiectasia, and systemic effects in certain cases. Consequently, healthcare authorities and professional organizations have increasingly emphasized the need for cautious prescribing, appropriate duration of therapy, and patient education.[60,61]

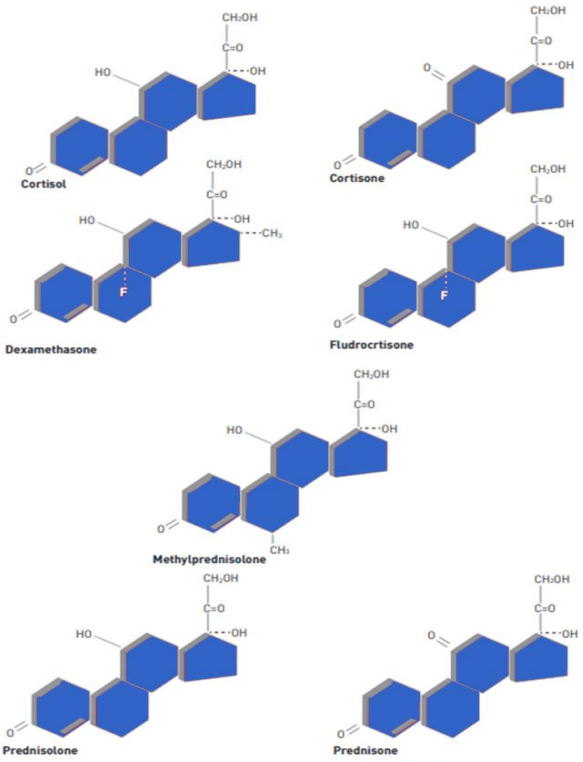


Figure 1. Structures of commonly prescribed synthetic glucocorticoids, and mineralocorticoid.

Pharmacokinetics

In circulation, cortisol exists in three distinct forms: free cortisol, protein-bound cortisol, and inactive metabolites .[64]Only a small proportion, nearly 5%, remains unbound and biologically active, while the majority is associated with plasma proteins such as corticosteroid-binding

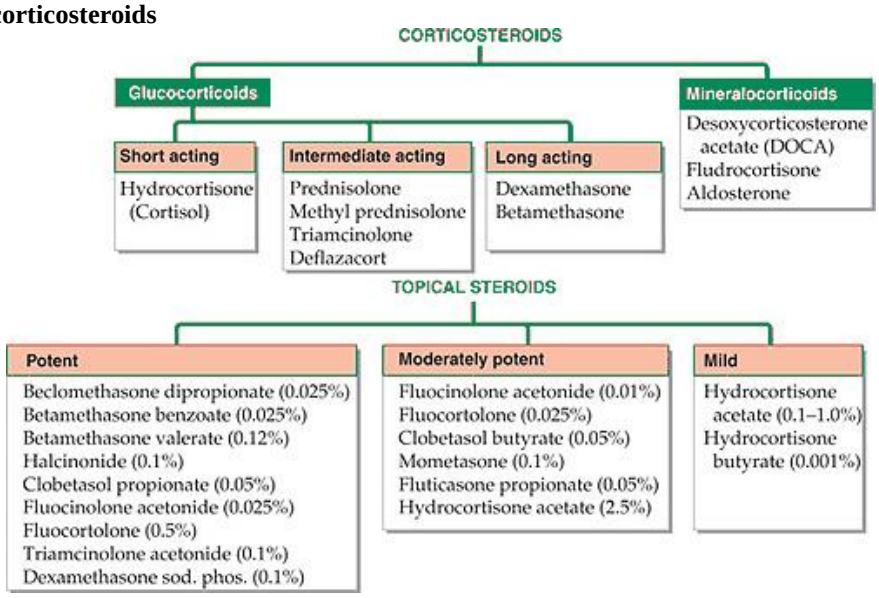
globulin and albumin. Under inflammatory conditions, the affinity of cortisol for these binding proteins decreases, resulting in an increased concentration of free cortisol at target tissues, thereby enhancing its anti-inflammatory effects. Synthetic corticosteroids also exhibit protein binding, although generally with lower affinity compared to endogenous cortisol. In contrast, cortisol metabolites lack biological activity and demonstrate minimal interaction with plasma proteins. The structural basis of corticosteroid activity was elucidated through chemical studies conducted during the mid-twentieth century. Cortisol possesses a characteristic steroid backbone composed of four interconnected rings three six-membered rings and one five-membered ring collectively known as the cyclopentanoperhydrophenanthrene nucleus. The molecule contains 21 carbon atoms, including a side chain attached to the 17th carbon and methyl substitutions at positions 10 and 13. Modifications to this fundamental structure have enabled the synthesis of various corticosteroid analogues with enhanced or altered pharmacological properties.[65]

For example, oxidation at the 11th carbon produces cortisone, whereas the introduction of a double bond between the first and second carbon atoms leads to the formation of prednisolone. Further chemical modification, such as methyl substitution at the sixth carbon, results in methylprednisolone. Additional structural changes, including fluorination at the 9-alpha position, have been shown to increase glucocorticoid potency, as observed in agents such as dexamethasone and betamethasone. Certain corticosteroids, including cortisone and prednisone, function as prodrugs and require metabolic conversion to their active forms before exerting therapeutic effects. Even minor alterations in molecular configuration can significantly influence the potency, duration of action, and mineralocorticoid activity of these compounds.[66]

Pharmacodynamic of corticosteroids

Corticosteroids exert potent anti-inflammatory and immunosuppressive effects by modulating multiple pathways involved in immune activation. Their primary action targets cell-mediated immune responses. These drugs bind to intracellular glucocorticoid receptors, leading to alterations in gene expression that suppress antigen presentation, decrease cytokine production, and inhibit the proliferation of lymphocytes. One of the early hematological effects observed after corticosteroid administration is a reduction in circulating lymphocytes. This decrease occurs due to redistribution of lymphocytes from the peripheral blood to lymphoid tissues rather than cellular destruction. The effect is usually evident within a few hours and reverses within 24 to 48 hours. Similarly, corticosteroids reduce the number of monocytes and eosinophils at inflammatory sites, thereby limiting their contribution to the inflammatory process. In contrast, corticosteroids increase circulating neutrophil levels. This phenomenon is attributed to enhanced release of neutrophils from the bone marrow, reduced migration into tissues, and decreased adherence to vascular endothelium. As a result, neutrophils accumulate in the bloodstream while their movement toward sites of inflammation is diminished. At the biochemical level, corticosteroids stimulate the production of lipocortin-1, which inhibits phospholipase A2 activity. This action prevents the release of arachidonic acid, thereby reducing the synthesis of key inflammatory mediators such as prostaglandins and leukotrienes. Additionally, corticosteroids suppress cyclooxygenase enzyme activity, further limiting prostaglandin production. Through these coordinated mechanisms, corticosteroids effectively downregulate inflammation and immune responses.[67,68]

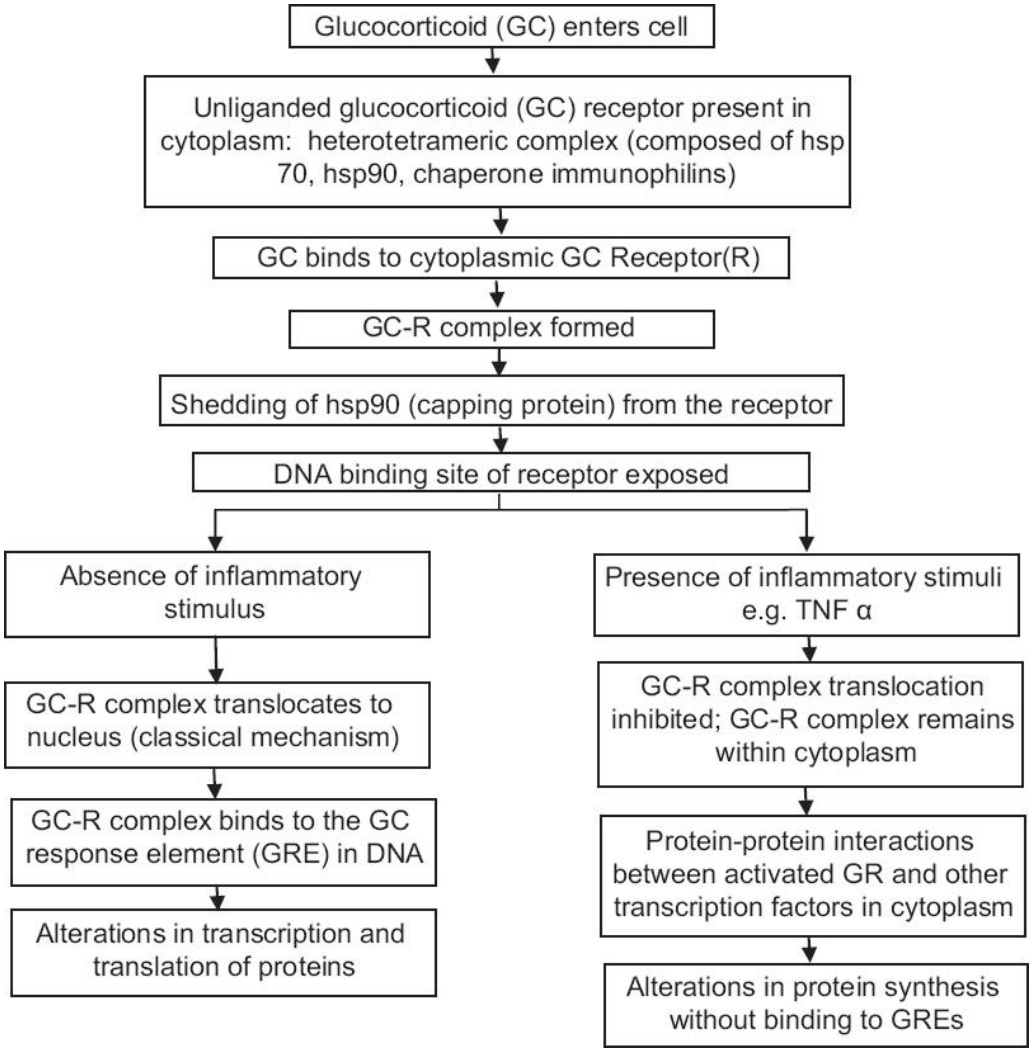
Classification of corticosteroids



Topical corticosteroids

The growing use of topical corticosteroids can be attributed to their rapid therapeutic action and effectiveness across a broad spectrum of dermatological conditions, including atopic dermatitis, psoriasis, lichen planus, and autoimmune blistering disorders. Drug-related factors such as high potency, quick symptomatic relief, wide availability, and the presence of fixed-dose combinations with antimicrobial agents further contribute to their extensive use. Patient-related factors also play a role, particularly the use of these agents for cosmetic purposes such as skin lightening and pigmentation control, especially among women. Additionally, prescribing practices influence usage patterns, as potent corticosteroids are often inappropriately recommended even for mild skin conditions. The adverse effects associated with topical corticosteroids vary depending on the extent of application, duration, and frequency of use. Prolonged and unsupervised application can result in significant complications, particularly when applied to sensitive areas like the face and genital region, where higher absorption enhances the risk of toxicity. In the Indian context, misuse is further driven by over-the-counter availability and limited access to dermatological care in rural settings. The frequent combination of corticosteroids with antibiotics, antifungals, and depigmenting agents also promotes irrational use.[69,70]

Mechanism of action



Indications

The therapeutic response to topical corticosteroids varies depending on the nature of the dermatological condition. Disorders that respond readily to treatment can be effectively managed with low- to moderate-potency agents. Conditions with partial responsiveness may require stronger formulations, sometimes combined with occlusive therapy to improve drug penetration.[71] In contrast, resistant dermatoses may necessitate the use of very potent topical corticosteroids or administration through intralesional routes. Topical corticosteroids continue to be a cornerstone in the management of inflammatory skin disorders such as eczema, where they are often indispensable. They are also widely used in localized vitiligo due to their favorable response rates. Additionally, potent corticosteroids like clobetasol have

demonstrated superior efficacy compared to calcineurin inhibitors such as tacrolimus in certain conditions, including vulvar lichen sclerosus.[72]

Topical Corticosteroid (TCS) Prescribing Guidelines

Appropriate prescribing of topical corticosteroids is essential to maximize therapeutic benefits while minimizing potential risks. A structured and patient-centered approach helps ensure safe, effective, and rational use of these agents in dermatological practice.

Selection of Potency

The selection of a topical corticosteroid should follow the principle of using the lowest effective potency required to control the disease. This reduces the likelihood of adverse effects, including skin atrophy and steroid withdrawal reactions. Mild corticosteroids are preferred for sensitive areas such as the face, flexures, and genital regions, whereas more potent agents may be required for thicker skin areas like the palms and soles or in severe dermatoses. Treatment is generally initiated with once-daily application. If the response is inadequate after 1–2 weeks, the frequency may be increased to twice daily for a short duration. Escalation to higher-potency corticosteroids should be reserved for resistant cases and should always be time-limited.[73]

Appropriate Quantity and Method of Application

Patients should be advised to apply a thin, even layer of the medication to the affected area and gently rub it in until fully absorbed. Over-application does not improve efficacy but significantly increases the risk of adverse effects. The Fingertip Unit (FTU) method should be explained to standardize dosing. This method helps patients understand the exact quantity required for different body regions, thereby improving adherence and reducing misuse. Healthcare professionals, including pharmacists, play a key role in reinforcing correct application techniques.[73]

Role of Adjunctive and Alternative Therapies

The use of adjunctive therapies can enhance treatment outcomes. Regular application of emollients alongside corticosteroids helps restore the skin barrier, improve hydration, and reduce the need for prolonged steroid use. In certain cases, non-steroidal agents such as topical calcineurin inhibitors may be preferred, particularly for long-term maintenance or use in sensitive areas. Combination therapy strategies, including intermittent corticosteroid use with continuous moisturization, have been shown to reduce relapse rates and improve overall disease control.[73,74]

Stepwise Approach to Prescribing

A systematic approach should be followed to ensure rational use

- **Establish diagnosis:** Confirm the dermatological condition through proper clinical evaluation.
- **Select appropriate agent:** Consider factors such as site of involvement, severity, patient age, and disease responsiveness. Opt for the least potent effective agent.
- **Define treatment plan:** Determine duration, frequency of application, choice of formulation (ointment, cream, lotion), and extent of body surface area to be treated.
- **Educate the patient:** Provide clear instructions on dosage (using FTU), application technique, duration, and expected outcomes.
- **Monitor response:** Regular follow-up is essential to assess improvement and detect early signs of adverse effects.
- **Modify therapy:** Adjust treatment based on response—this may include stepping up therapy for inadequate control or stepping down once remission is achieved. Re-evaluation of diagnosis should be considered if expected outcomes are not observed.

Additional Practical Considerations

- Prefer once-daily application when possible, as it improves compliance without compromising efficacy.
- Use short treatment courses for acute flares and avoid continuous long-term use of potent steroids.
- Special caution is required in children and elderly patients due to increased susceptibility to systemic absorption and side effects.
- Avoid using potent corticosteroids on thin skin areas unless absolutely necessary.
- Document treatment plans clearly to prevent misuse and ensure continuity of care.

Use in Pregnancy

Topical corticosteroids are generally categorized under pregnancy risk category C, indicating that their use should be based on a careful assessment of benefits versus potential risks. Current evidence does not conclusively link their use to major adverse pregnancy outcomes such as congenital anomalies, preterm birth, or fetal loss. However, prolonged use of high-potency formulations may be associated with reduced birth weight, although the supporting evidence remains limited and requires further validation.[75,76]

Selection, Application, and Frequency

The selection of an appropriate corticosteroid preparation depends on multiple factors, including the site of application, severity and extent of the condition, patient age, and the formulation used. Areas with thinner skin, such as the face, eyelids, and intertriginous regions, require milder preparations to minimize adverse effects. Similarly, low-potency corticosteroids are preferred in pediatric patients and when treating large surface areas. Topical corticosteroids exhibit a sustained effect due to their retention within the skin layers, often referred to as a reservoir effect. This characteristic may reduce the need for frequent application. Evidence suggests that once-daily use can be as effective as multiple daily applications in many cases. Some studies indicate that the drug may remain active within the skin for several

days, although further research is needed to establish optimal dosing frequency.[77]

Factors Influencing Choice

Several considerations guide the selection of topical corticosteroids, including:

- Site of involvement
- Responsiveness of the condition
- Severity of disease
- Extent of affected surface area
- Age of the patient
- Type of formulation
- Potency of the corticosteroid[78]

Dosage Measurement: Fingertip Unit Method

To ensure accurate dosing, the fingertip unit (FTU) method is commonly employed. One FTU is defined as the amount of ointment expressed from a standard tube applied from the fingertip to the distal crease of the index finger, approximately equal to 0.5 g. Another practical guideline, known as the "rule of hand," suggests that the area equivalent to one side of an adult hand requires about 0.5 FTU (approximately 0.25 g). In simple terms, four hand-sized areas correspond to around 1 g of topical preparation.

Estimated FTU requirements for different body regions in adults include

- Face and neck: ~2.5 FTUs
- Trunk (front and back): ~14 FTUs
- Each upper limb: ~3 FTUs
- Each hand: ~1 FTU
- Each lower limb: ~6 FTUs
- Each foot: ~2 FTUs

This standardized approach helps improve treatment accuracy, patient understanding, and overall therapeutic outcomes.[73]

Duration of Use

The use of topical corticosteroids should be limited to the shortest duration necessary to achieve clinical improvement. Highly potent agents such as clobetasol propionate and halobetasol propionate are generally recommended for short-term therapy, usually not exceeding two weeks. To minimize the risk of systemic toxicity, weekly quantities should remain within safe limits, typically around 50 g for halobetasol and 60 g for clobetasol. Similarly, the use of potent corticosteroids like betamethasone dipropionate should be restricted to moderate weekly amounts. Extended use of high-potency corticosteroids or their application under occlusion is generally avoided due to enhanced absorption and increased likelihood of adverse effects. After initial control of symptoms, it is advisable to gradually reduce treatment intensity by switching to lower-potency agents or non-steroidal alternatives. Maintenance strategies, including intermittent or weekend therapy, may help sustain remission while minimizing risks.[80]

Wet-Wrap Therapy and Soaks

Wet-wrap therapy is an adjunctive treatment technique used to improve the efficacy of topical corticosteroids. It involves applying the medication to affected skin followed by covering the area with a moist layer and then a dry outer layer. This method enhances hydration, improves drug penetration, and provides symptomatic relief, particularly by reducing itching and inflammation. This approach is especially beneficial in acute exacerbations of atopic dermatitis in children. It has also been applied in other inflammatory skin conditions such as chronic eczema, psoriasis, and pruritic disorders. While several studies suggest improved short-term outcomes with this technique, differences in methodology make it difficult to establish uniform conclusions. Careful supervision is necessary to prevent complications such as infection or excessive systemic absorption.[81,82]

Tachyphylaxis and Bradyphylaxis

A decline in therapeutic response during prolonged corticosteroid use has often been described as tachyphylaxis, which refers to a rapid decrease in drug effectiveness after repeated use. However, strong clinical evidence supporting this concept in topical corticosteroids is limited. In many dermatological conditions, especially psoriasis, the beneficial effects are primarily due to anti-inflammatory and immunosuppressive actions rather than mechanisms that typically lead to drug tolerance.[83] In clinical practice, an apparent reduction in efficacy is more commonly linked to factors such as poor adherence to treatment or the natural progression of the disease. Patients often show marked improvement initially, followed by a plateau phase where further progress is minimal. Fluctuations in disease activity during this phase may give the impression of reduced drug effectiveness. The term "bradyphylaxis" has been introduced to describe a gradual and progressive decline in response over extended periods. This highlights the importance of treatment optimization strategies such as rotation of therapies, intermittent dosing, and patient education to maintain long-term effectiveness.[84]

Adverse Effects

Topical corticosteroids are associated with both local and systemic adverse effects, the likelihood of which depends on factors such as potency, duration of use, and area of application. Local adverse effects may include burning, irritation, and dryness shortly after application. Prolonged use can result in thinning of the skin, pigmentation changes, increased sensitivity to sunlight, and weakening of the skin barrier. Structural changes in the dermis, including reduced collagen production, may lead to telangiectasia, striae, easy bruising, delayed wound healing, and atrophy. Additional complications include steroid-induced acne, rosacea, abnormal hair growth, and hair loss. These medications may also predispose to infections or alter their clinical appearance, leading to atypical presentations of fungal, bacterial,

parasitic, and viral infections. Other reactions include perioral dermatitis, allergic contact dermatitis, urticaria, and granulomatous conditions. Sudden discontinuation after prolonged use can result in rebound flares of underlying diseases, such as psoriasis or severe facial erythema.[85]

Chronic misuse has been linked to conditions like steroid-dependent dermatitis and red skin syndrome. Systemic effects are uncommon but may occur with prolonged use of potent corticosteroids, especially when applied over large areas or under occlusion. These include suppression of the hypothalamic–pituitary–adrenal axis, elevated blood glucose levels, Cushingoid features, fluid retention, and hypertension. In children, growth suppression may occur, while adults may be at risk of bone-related complications such as osteoporosis. Ocular complications, including cataracts and glaucoma, may develop, particularly with use near the eyes. Preventive measures include selecting the appropriate potency, limiting duration, reducing frequency after improvement, avoiding unnecessary occlusion, and ensuring proper patient education.[86]

Strategies to Minimize Adverse Effects

Preventing side effects is a critical component of therapy. Patients should be instructed to avoid applying corticosteroids to unaffected areas and to wash their hands after application to prevent inadvertent spread, especially to the face. Prolonged or inappropriate use may lead to complications such as acne, perioral dermatitis, and skin thinning due to reduced collagen synthesis. This can result in telangiectasia, striae, and increased susceptibility to bruising. Limiting the duration of therapy, using the lowest effective potency, and avoiding occlusion unless specifically indicated are key preventive measures. In addition, gradual tapering rather than abrupt discontinuation is recommended to prevent rebound flares and withdrawal reactions.[87,89]

Importance of Vehicle Selection

The formulation of topical medications significantly influences treatment outcomes. Different vehicles—such as ointments, creams, lotions, and gels—affect drug absorption, hydration, and patient acceptance. Ointments tend to enhance penetration due to their occlusive nature, while creams and lotions are often preferred for ease of application and cosmetic acceptability. In some cases, components of the formulation may irritate the skin or disrupt the skin barrier. Both the active drug and inactive ingredients can contribute to hypersensitivity reactions. Therefore, selecting an appropriate formulation tailored to the patient's condition and skin type is essential. Advances in formulation technology have led to improved delivery systems that enhance efficacy while minimizing irritation and improving patient adherence.[90,92]

Contact Allergy to Topical Corticosteroids

Allergic reactions to topical corticosteroids are increasingly being identified in clinical settings. The estimated prevalence ranges from a small percentage to several cases per hundred individuals. This condition should be suspected when expected therapeutic outcomes are not achieved or when symptoms worsen despite appropriate treatment. The allergic response may be triggered by the active corticosteroid molecule, inactive ingredients such as preservatives or vehicles, or even materials used in packaging.[90] The underlying mechanism involves the formation of reactive compounds that bind to skin proteins, initiating an immune response. Non-halogenated corticosteroids are generally considered more likely to cause such reactions compared to halogenated ones, possibly due to differences in molecular stability. Corticosteroids are grouped structurally to help predict cross-reactivity during diagnostic testing. These groups include hydrocortisone-type, triamcinolone-type, betamethasone-type, and hydrocortisone butyrate-type compounds. Patch testing is useful in identifying the causative agent and guiding alternative treatment options.[91,92]

Corticosteroids with Improved Safety Profile

Recent advancements in drug design have resulted in newer topical corticosteroids with improved safety and efficacy. Chemical modifications, particularly the development of esterified molecules, have enhanced anti-inflammatory properties while reducing systemic absorption and local adverse effects. Many of these newer agents are non-halogenated double esters, which offer a better balance between therapeutic benefit and safety. Examples include prednicarbate, methylprednisolone aceponate, mometasone furoate, and hydrocortisone aceponate.[92] Prednicarbate is associated with effective anti-inflammatory action and minimal risk of skin atrophy, making it suitable for sensitive populations such as children and older adults. Fluticasone propionate provides potent anti-inflammatory effects with low systemic availability and minimal risk of hormonal suppression. Mometasone furoate combines strong efficacy with reduced potential for systemic side effects and allows convenient once-daily application. Methylprednisolone aceponate is recognized for its high therapeutic effectiveness, low atrophogenic potential, and minimal impact on endogenous cortisol levels.[94]

Patient Education and Adherence

Patient awareness and understanding are crucial for successful therapy. Many individuals have concerns regarding the safety of topical corticosteroids, which may lead to underuse or non-compliance. Clear counselling should address these fears and emphasize the importance of adhering to prescribed regimens. Patients should also be warned against prolonged or unsupervised use, as this may lead to dependency, rebound flares, or masking of underlying conditions. Accurate diagnosis

should always be confirmed before initiating therapy to avoid inappropriate treatment.[95,97]

CONCLUSION

Corticosteroids continue to play a vital role in the management of inflammatory skin diseases due to their strong therapeutic efficacy. However, their benefits must be balanced with potential risks associated with inappropriate or prolonged use. Rational prescribing, appropriate potency selection, and patient education are essential to ensure safe and effective treatment. Emerging formulations with improved safety profiles offer promising alternatives for long-term management. Ultimately, a patient-centered and evidence-based approach, combined with regular monitoring, can optimize clinical outcomes while minimizing adverse effects. Strengthening awareness among healthcare professionals and patients is crucial to reduce misuse and promote the responsible use of corticosteroids in dermatology.

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