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Investigating Subclinical Elastosis in Long-Term Steroid Use and Its Contribution to Skin Thinning

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ABSTRACT

Long-term corticosteroid use is a well-documented cause of skin thinning, with subclinical elastosis emerging as an important yet underexplored mechanism contributing to this phenomenon. Corticosteroids impact skin structure and function through multiple pathways, including inhibition of fibroblast activity, reduced collagen synthesis, and dysregulation of extracellular matrix remodeling. Recent evidence suggests that elastin metabolism is also significantly affected, leading to the accumulation of fragmented and non-functional elastic fibers, a condition referred to as subclinical elastosis. Abnormal elastin deposits disrupt the mechanical integrity and resilience of the dermis, exacerbating skin thinning and increasing susceptibility to tears and bruising. Corticosteroid-induced oxidative stress and impaired matrix metalloproteinase regulation amplify elastin degradation and remodeling defects, creating a pro-elastotic environment. Subclinical elastosis is particularly pronounced in chronic users of topical and systemic corticosteroids, with histological studies revealing early dermal changes that precede visible thinning. Diagnostic advancements, such as high-resolution imaging and elastography, are improving the detection of these subtle alterations, offering insights into the progression of steroid-induced skin changes. Therapeutic approaches aimed at mitigating subclinical elastosis focus on restoring extracellular matrix balance through agents that promote fibroblast activity, enhance collagen production, and modulate elastin synthesis. Adjunctive therapies, such as antioxidants and topical growth factors, show potential in counteracting oxidative damage and preserving dermal architecture. Understanding subclinical elastosis in steroid-induced skin

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thinning provides a foundation for developing targeted strategies to prevent and treat this condition, ultimately improving skin health outcomes in patients requiring long-term corticosteroid therapy.

Keywords: Corticosteroids, Skin Thinning, Subclinical Elastosis, Fibroblast Inhibition, Collagen Synthesis, Extracellular Matrix Remodeling, Elastin Metabolism

INTRODUCTION

Long-term use of corticosteroids remains the cornerstone of management in numerous inflammatory conditions. Despite their undeniable efficacy, the long-term administration of steroid medications is fraught with a host of side effects, among which cutaneous complications remain the most prevalent. Thinning of the skin has been mentioned as a sequela; despite this, the exact mechanisms elude clinicians and researchers even years since the recognition of the same [1,2]. Inflammatory diseases are usually chronic; however, skin atrophy may develop after only six weeks of therapy and result in up to 59% reduction in epidermis thickness. This seriously compromises skin integrity and its structure. While the prevalence of inflammatory diseases continues to increase, there is an emerging need for effective and safe long-term therapy.

Subclinical elastosis, a previously underexplored mechanism, is emerging as a significant contributor to skin thinning. Elastosis refers to the deposition of abnormal and dysfunctional elastin fibers that reduce the integrity of the skin, hence making it further vulnerable. Corticosteroids inhibit fibroblast activity and extracellular matrix remodeling by depleting mucopolysaccharides and elastin, leading to elastosis [1]. Although similar processes can be observed in sun exposure and aging of the skin naturally, corticosteroids accelerate the problem. Routine examination of the epidermis with light usually can reveal some disorders resulting from the application of corticosteroids, while more sensitive imaging modalities are capable of detecting them earlier. Even prior to when the thinning of skin is clinically visible, imaging modalities like multiphoton microscopy reveal that the elastin has already mutated [3]. This depicts early detection of the dermis and epidermis abnormality. The advanced imaging modality provides much enhancement of such subclinical modification detection and makes it capable of observing, researching, and studying early dermal alteration to a more understandable stage, which then opens a treatment scope.

Previous therapies involved modification of corticosteroid treatment intervals, but even after almost a week of intermission between treatments, loss of skin thickness is still significant [4]. Current therapeutic strategies target the extracellular matrix and promote balance and regulation. Promising treatments promote fibroblast activity, exchange collage production, and alter elastin synthesis by targeting genes that inhibit collagen synthesis [5]. Adjuvant therapies also appear to suppress enzymes, originally known for their involvement in cortisol activation, that have been shown to increase collagen content and promote the proliferation of fibroblasts, suggesting possible therapy targets [6]. These new approaches emphasize the growing understanding of subclinical elastosis as a key target in managing dermal thinning.

Elucidation of these mechanisms will provide a better understanding of how to prevent and reverse damage. We aim to provide a framework for recognizing subclinical elastosis as a critical aspect of the advancement of long-term corticosteroid therapy. We collected and organized recent evidence, diagnosis, and therapeutic interventions to achieve this. New therapies to address dermal thinning also target the extracellular matrix-stimulating fibroblast activity and modulating collagen and elastin synthesis. These approaches are based on highlighting subclinical elastosis as an important target of therapy, possible through gene modulation and enzyme suppression to improve skin integrity. Results from such studies can further augment patient outcomes through a balance of benefits from corticosteroid therapy with avoidance of its noxious dermatological side effects.

CORTICOSTEROID IMPACT ON ELASTIN METABOLISM

Corticosteroids, widely utilized in dermatological therapeutics for their potent anti-inflammatory properties, significantly alter elastin metabolism, a critical component of skin architecture and function. Prolonged exposure to corticosteroids is associated with the accumulation of fragmented and non-functional elastic fibers within the dermal matrix [7]. This disruption in elastin homeostasis results in a condition referred to as subclinical elastosis. Although often asymptomatic in its early stages, elastosis can profoundly affect cutaneous integrity and resilience [8]. Elastin, an essential protein within the extracellular matrix, plays a crucial role in maintaining skin elasticity and structural integrity [7]. Disturbances in elastin metabolism—whether caused by intrinsic factors such as

genetic predisposition and aging or extrinsic factors such as UV exposure and pollution—lead to architectural changes that compromise biomechanical properties. These disruptions result in alterations in elastin architecture, affecting skin elasticity and tensile strength, ultimately contributing to epidermal thinning [8].

Subclinical Elastosis and Dermal Integrity

Subclinical elastosis is characterized by the disorganization of elastin fibers within the skin, leading to a loss of elasticity and tensile strength. This degradation compromises the mechanical integrity of the dermis, leaving the skin more susceptible to mechanical tension, abrasions, bruising, and poor wound healing [8]. Such disruptions not only affect the skin's physical properties but also impair cellular activity within the dermal environment. Resident fibroblasts, responsible for producing collagen and elastin, exhibit altered behavior in response to changes in elastin structure [7]. These fibroblasts may release inflammatory mediators, including cytokines and growth factors, which perpetuate local inflammation and attract immune cells. This inflammatory cascade further exacerbates skin vulnerability.

Corticosteroid-Induced Inflammatory Cascade

The disruption of elastin metabolism initiates a cascade of inflammatory responses, compounding skin vulnerability [7]. Beyond inflammation, changes in elastin architecture alter the skin's biomechanical properties and exacerbate fibroblast dysfunction. Chronic inflammation and impaired healing can lead to severe outcomes, such as dermatitis and skin atrophy, marked by thinning and structural loss [8,9]. This weakened barrier function makes the skin more susceptible to irritants, pathogens, and injury.

Mechanistic Insights into Corticosteroid-Induced Damage

According to Lehmann et al. (1983), corticosteroids negatively impact elastin metabolism by interacting with cells responsible for elastin production, inhibiting its synthesis, and promoting degradation [8]. In a study involving healthy, college-age volunteers, significant changes in collagen structure were observed 4 to 5 weeks after corticosteroid treatment. Collagen fibril diameter was reduced, indicating defective synthesis or assembly, and disorganized bundle formation weakened overall skin architecture. The degeneration of elastic fibers under corticosteroid treatment mimics processes typically associated with natural skin aging, causing premature signs of aging even in younger individuals [8]. Such changes reflect wider ramifications, including increased susceptibility to injury, reduced wound-healing capabilities, and long-term alterations in skin appearance and function.

Electron Microscopy Observations

Electron microscopy has revealed marked changes in elastic fibers following corticosteroid treatment. In untreated skin, subepidermal elastic fibers exhibit a perpendicular, branching, or candelabra-like orientation, with fiber tips nearly touching the basement membrane [8]. These healthy fibers are thick, coarse, and typically oriented horizontally. After three weeks of topical steroid treatment, a significant loss of the perpendicular, vertical arrangement of elastic fibers within the subepidermal papillary zone was observed [8]. The degree of elastin disorganization correlated directly with the duration of steroid use, indicating a dose-dependent relationship. Prolonged or increased exposure to topical steroids results in cumulative damage to elastic fibers, emphasizing the need for careful monitoring during dermatological treatments [9].

The alterations in elastin metabolism and fiber architecture caused by corticosteroids highlight the delicate balance between their therapeutic efficacy and their impact on skin structural integrity. The dose-dependent nature of elastic fiber degradation underscores the importance of cautious corticosteroid use, particularly in long-term treatments. This understanding calls for the development of strategies to minimize corticosteroid-induced damage while maintaining their anti-inflammatory benefits.

PATHOPHYSIOLOGY OF SKIN THINNING ASSOCIATED WITH GLUCOCORTICOID USE

Systemic corticosteroids profoundly affect skin homeostasis through systemic effects beyond the anti-inflammatory action. Regarding the main mechanisms of skin thinning, inhibition of fibroblast activity causes a disruptive effect on collagen synthesis and extracellular matrix remodeling. Fibroblasts are one of the major cell types responsible for collagen and elastin production, providing strength and elasticity to the skin. Suppression of fibroblast activity results in an overall diminished synthesis of collagen, which would therefore weaken dermal structure and lead to an increased fragility of the skin [10,11]. Moreover, corticosteroids interfere with elastin metabolism by causing deposition of

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fragmented nonfunctional elastin fibers, otherwise referred to as subclinical elastosis [12]. This accumulation undermines the mechanical integrity of the dermis, making it far more susceptible to bruising, tears, and visible signs of aging.

Dysregulation of matrix metalloproteinases plays another important role in corticosteroid-induced skin thinning. It is an enzyme involved in the remodeling of the ECM. Corticosteroids promote a pro-elastotic environment through enhancement of elastin degradation rather than proper synthesis and remodeling. Dysregulated MMP activity perpetuates this imbalance, leading to elastin degradation and a failure to maintain functional elastin fibers. These alterations, compounded by oxidative stress from long-term corticosteroid use, significantly impair the dermal matrix [13,14]. Oxidative stress, characterized by excessive reactive oxygen species (ROS), damages cellular components and accelerates elastin degradation, creating a vicious cycle of structural damage. Histological studies reveal that significant dermal changes occur early in corticosteroid therapy, often preceding clinically visible skin thinning. Early dermal alterations include disrupted fibroblast activity and impaired ECM integrity, highlighting the need for proactive monitoring of patients undergoing glucocorticoid therapy [11,15]. High-resolution imaging techniques, including elastography, allow for real-time skin elasticity assessment and early detection of corticosteroid-induced damage. Such diagnostic capabilities have the potential to enable timely interventions that could avoid irreversible skin thinning.

Glucocorticoid Dose-Adverse Event Relationship

In a population-based survey of 6,517 individuals, the prevalence of AEs related to long-term glucocorticoid use was investigated [11]. This dose-related pattern in AE was documented. The most frequently encountered complication reported in the questionnaires was a weight gain almost from 80% of respondents who were using it in the highest quartile. The remaining, frequently described AEs include thinning of skin and disturbance of sleep, whereas cataracts at 15% and fractures at 12% account for less common but clinically more relevant AEs. Interestingly enough, only a few patients -10%- with glucocorticoid treatment do not experience AEs. Analysis of fracture-related claims data underlined the bone-related risks as well: "10% of this cohort received medical services for fractures in a 30-month observation period" [11]. Of the AEs reported, skin thinning is a complication of particular concern because of its profound impact on dermal structure and function. Prolonged corticosteroid use enhances oxidative stress, which accelerates elastin degradation and impairs elastin synthesis. The result is dermal fragility and thinning, with early subclinical changes often going undetected until damage is irreversible [13,14]. The findings highlight the need for regular monitoring and dose adjustments to prevent such complications.

Therapeutic Interventions and Clinical Implications

Counteracting strategies to corticosteroid-induced skin thinning include the restoration of ECM balance and mitigation of oxidative damage. Both topical growth factors and antioxidants hold promise for overcoming these two challenges. Growth factors may trigger the activity of fibroblasts, resulting in increased synthesis of collagen to help restore strength in the dermis. The role of antioxidants involves the neutralization of ROS, thus preventing damage to collagen and elastin [12,14]. The mentioned therapeutic approaches along with advances in diagnostic techniques such as elastography may provide the way for early detection and interference. Clinical practice should be to educate the patient about the possibilities of AEs of glucocorticoids, holding a discussion on risks for long-term therapy. Monitoring should be regularly performed for complications weight gain, thinning of the skin, or sleep disturbances. Elucidation of pathophysiological mechanisms for AEs allows clinicians to find a focused strategy to minimize their impact and ensure better patient outcomes when receiving long-term glucocorticoids [11,15]. Through a combination of patient education, vigilant monitoring, and targeted interventions, clinicians can balance therapeutic efficacy with the prevention of adverse effects.

DIAGNOSTIC APPROACHES

Importance of Physical Examination and Diagnostic Technology

The physical exam with palpation and observation has been a cornerstone of clinical evaluations since the earliest days of medicine and remains a vital tool for evaluating skin integrity following treatment. High-frequency ultrasound (HFUS) is the most established and studied diagnostic tool for quantifying corticosteroid-induced skin atrophy and dermal thickness changes with studies dating back to the 1980s [16]. Before ultrasound, other noninvasive methods included the Harpenden skinfold caliper, radiological techniques, and

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the ratchet-controlled micrometer [17]. As the introduction of the pulse technique with ultrasounds grew popular, the use of xeroradiography started to decline. The ultrasound consistently showed a greater degree of thinning following corticosteroid treatment and was more accurate, allowing for the small changes to be identified earlier [17]. Due to its effectiveness, the technology and advancement of the technique and its utilization continued to progress. In addition, ultrasound has been so useful due to its many advantages including its non-invasive nature, low cost, real-time images, and availability.

Visualization of Skin Layers with Ultrasound

On ultrasound, the three layers of skin can be visualized due to their distinct echogenicity. The epidermis is hyperechoic due to the keratin strongly reflecting sound waves, the dermis is slightly less hyperechoic due to the high content of collagen, and the subcutis is hypoechoic due to the fat lobules. Breaking it down further, the upper 20% of the dermis corresponds to the papillary dermis with the irregular arrangement of thinner collagen and elastin bundles. The lower 80% holds the more structured collagen and elastin [18]. The ability to visualize the separation of the layers of the dermis allows clinicians a view of the integrity of the elastin since elastosis will decrease skin echogenicity.

EMERGENCE OF ADVANCED DIAGNOSTIC TOOLS: ELASTOGRAPHY AND OPTICAL COHERENCE TOMOGRAPHY

With advancements in diagnostic technology, the clinical assessment of skin health has become increasingly more specific and efficient. Several diagnostic methods have emerged that allow for quick identification of thinning, imaging, and quantitative information on the physical properties of tissue alterations such as ultrasound elastography (USE) and optical coherence tomography (OCT). Meaning, these modalities can provide information on the degree of skin elasticity following various treatments. In recent years, the technique of HFUS has expanded to include elastography. While HFUS alone has proven to be effective in determining dermal thickness variation following steroid treatment, it has been reported that the dermal mechanical properties vary to a greater extent, 35% and 10%, respectively [19]. Therefore, using elastography to identify the mechanical properties of the elastin bundles in the dermis may provide more quality information on the side effects of steroid treatment. The first landmark review was published in 1996, which opened up the era of ultrasonic imaging of soft tissue straining and elasticity [20]. Since then, multiple reviews have been published to expose the opportunities elastography can provide in both clinical surveillance and research.

Elasticity and Tissue Stiffness

Whenever a physiologic or pathologic alteration occurs to the skin, there is some rebound effect on the surrounding tissues. When subjected to pressure, tissue deforms, and the tendency for it to recover to its initial shape after removal of the pressure is referred to as elasticity [21]. Tissue stiffness refers to the resistance to the deformation. During USE, external pressure is applied either by manual compression or acoustic radiation forces, and the stiffness is measured by the magnitude of the tissue deformation. The two types of elastography include strain elastography (SE) and shear wave elastography (SWE). SE measures the physical tissue displacement parallel to the applied stress, and SWE utilizes dynamic stress to generate a shear wave in the perpendicular dimensions [22]. The ability to produce real-time images with measurements of the degree of varying stiffness and elasticity allows for effective assessment of disease progression or the effects of steroid treatments.

Optical Coherence Tomography (OCT)

Optical coherence tomography is another high-resolution, non-invasive imaging technique that can advance the diagnostic sophistication of subclinical elastosis. OCT is a light-based interferometry that provides a digital image of the skin and allows for a quantitative evaluation of epidermal thickness [23,24]. Without ever having to touch the surface of the skin, multiple two-dimensional cross-sectional images are produced in real-time that allow visibility to the characterization of the epidermis. This technique was first used to measure eye length, and assess ophthalmic diseases, and was often referred to as an optical biopsy since it provided histological information non-invasively [23]. It has been proven to be a highly sensitive technique for assessing corticosteroid-induced skin atrophy [25]. Since damage first occurs in the epidermis from corticosteroids, some researchers argue that OCT is a more appropriate diagnostic tool than HFUS. When evaluating the anthropogenic potential of glucocorticoids, Cobmann et al. compared OCT and HFUS and found that while they both allowed for the detection and monitoring of skin atrophy, the epidermal atrophy could be detected earlier by OCT than the reduction of dermal thickness assessed by ultrasound [16]. While this imaging modality may not provide

specific data on elasticity following treatment, it may be helpful to identify the negative clinical progression of the skin at the earliest point in treatment.

Applications and Limitations of Ultrasound Elastography

Currently, the best validated application of USE is to assess liver fibrosis. Other well-documented uses include quantification of portal hypertension, breast lesion characterization, and the assessment of kidney fibrosis, lymph nodes, and inflammatory skin diseases such as morphea and sclerosis [22]. Limitations of USE are similar to those associated with general sonography, including the technique being heavily dependent on the skill of the operator. Particularly with the compression strain elastograms, there is great potential for the amount of pressure applied to the site to vary with each use. Also, since this is a newer modality, there is no standard commercial system design and settings across manufacturers. The diagnostic field of imaging elastic tissue properties has evolved immensely over the past few decades and will continue to expand its clinical applications and commercial platforms, and standardize its technique. Especially since every deformable tissue, organ, and structure can be considered a potential application for elastography imaging [24]. By utilizing a combined approach with a well-established modality such as HFUS, elastography has the potential to identify the ideal balance between the maximum therapeutic impact of corticosteroids with the least amount of negative side effects.

Multiphoton Microscopy

Multiphoton microscopy (MM) is another newer diagnostic tool that allows for in-vivo simultaneous visualization of early corticosteroid-induced epidermis modifications. This technique has been utilized for cosmetic, pharmaceutical, and skin aging research; however, a few studies have identified its function in the assessment of corticosteroid use. Ait El Madani et al. illustrate how MM is impressive because it allows access to other changes in the epidermis that OCT cannot [3]. For instance, MM allows visualization of modifications induced in the cells or elastic and collagen fiber networks within the epidermis. OCT can quickly see changes in epidermal thickness, however, it lacks specificity and MM facilitates assessment of the changes within the smaller structures of the epidermis such as elastin via two-photon excited fluorescence signals and second harmonic generation signals [3]. This non-invasive technique allows for the continuous monitoring of epidermal changes in the elastic fiber network, thus it has the potential to identify subclinical elastosis at a quick and efficient rate. However, one limitation is the small field of view with visualization of the papillary dermis only.

High-frequency ultrasound, elastography, optical coherence tomography, and multiphoton microscopy are all proven methods of accurate identification of changes in normal skin architecture following corticosteroid treatment. Whether it is skin atrophy in the epidermis or dermis or specific data on the elasticity and stiffness of the skin, they all have the potential to provide a well-rounded assessment of the harsh side effects of treatment. Loss of elasticity or rigidity often correlates with poor outcomes in skin disease progression, therefore the advancement of these technologies to identify elastosis as accurately and early as possible will greatly benefit patients reliant on corticosteroids for treatment.

THERAPEUTIC STRATEGIES

Subclinical elastosis, often associated with long-term therapeutic use of corticosteroid drugs, can be defined by changes in the extracellular matrix manifesting as thinned skin devoid of elasticity. Thus, these therapeutic strategies re-establishing the integrity of ECM could have a lot of potential with respect to such mitigating impacts. One popular strategy has indeed been targeting of therapies toward fibroblast stimulating activity. The role of fibroblasts in synthesizing the primary elements of ECM, such as collagen and elastin, is crucial to the structure and function of the skin [26]. Increased activity of fibroblasts upregulates the synthesis of these ECM components, as reported by Plikus et al. (2021), leading to more resilient cutaneous tissue that is better able to resist the long-term effects of steroid use [26]. Other than enhancing the activity of fibroblasts, elastin modulators may offer a promising target for therapy against subclinical elastosis [7]. The action of an elastin modulator is executed through a reduction in the breakdown of elastin, thereby improving the integrity of the skin structure and, therefore, the general appearance of the skin tone. They maintain a balance between synthesis and degradation, adding to more robust and elastic skin. Therefore, therapies that restore ECM integrity, stimulate fibroblast activity, and reduce elastin degradation represent potential solutions for treating subclinical elastosis associated with prolonged steroid use.

Antioxidants and Growth Factors

Another critical therapeutic target involves counteracting oxidative damage to cutaneous tissues. ROS have been implicated in skin aging and thinning, especially in the context of long-term steroid use [27]. The excessive accumulation of ROS disrupts cellular repair mechanisms in both dermal and epidermal tissues, contributing to skin degradation. Antioxidants help prevent cellular damage and promote the stability of the ECM by neutralizing free radicals [28]. Hence, the use of antioxidants has been one proposed strategy for treating subclinical elastosis. Topical growth factors are yet another promising modality of treatment that can effectively stimulate dermal cell repair and regeneration [29]. Such growth factors will not only help in promoting skin tissue repair but also provide enhanced fibroblast activities to increase functional collagen and elastin production, thereby restoring skin integrity and further increasing its resistance to corticosteroid-induced destruction. Antioxidants and topical growth factors, together, complement each other in regard to use against corticosteroid-induced oxidative damage for the promotion of tissue repair and enhancement of the stability of the ECM. Such treatments can preserve skin appearance and function by targeting both the pathways of oxidative stress and cellular regeneration in patients on long-term steroid therapy. Restoration of ECM integrity, improvement of functioning fibroblasts, prevention of elastin degradation, and counteracting oxidative damage are the most promising therapies proposed for the treatment of subclinical corticosteroid-induced elastosis. Therapeutic options shall be aimed at skin degeneration mechanisms in maintaining better skin health, its appearance, and functionality with time.

IMPLICATIONS FOR LONG-TERM CORTICOSTEROID USERS

Chronic use of topical and systemic corticosteroids is highly associated with skin thinning and subclinical elastosis. The degree of impact is affected by age, body location, potency of the drug, and the amount of repeated use. Skin thinning is correlated with a reduction in cell size and cell layers caused by a lack of cell proliferation, collagen synthesis, and fibroblast growth [30]. Chronic users are impacted by epidermal and dermal layer modifications.

Histological studies have identified various changes on the skin dermis layer resulting from corticosteroid use. Dermal atrophy is caused by the direct inhibition of fibroblast proliferation, leading to a reduction in mast cells and various dermis-supporting compounds including mucopolysaccharides, elastin, matrix metalloproteases, and collagen [1]. Glucocorticoids have been shown to rapidly decrease mast cell degranulation, thereby decreasing histamine and calcium release [31]. By implicating mast cell concentration and dermal support, studies have shown increased skin barrier permeability to protein antigens, ultimately decreasing barrier function [32]. Early dermal changes emphasize a need for early detection of skin atrophy through advancements such as high-resolution imaging and elastography. Studies have shown that sheer wave elastography has been effective in early detection of subclinical skin involvement with the ability to also identify the degree of collagen deposition [33]. Additionally, high-resolution magnetic resonance imaging can be used to observe changes in the layers of the epidermis and dermis [34]. By identifying corticosteroid-induced dermal changes early, changes can be made to treatment plans to limit skin thinning and subclinical elastosis.

Research has shown that therapeutics can be used to prevent steroid-induced skin thinning. By adding collagen-synthesis-enhancing therapeutics to a corticosteroid regimen, studies in mice models have been able to eliminate dermal atrophy [35]. Agents such as tretinoin, tazarotene gel, and rapamycin have all been found to successfully prevent glucocorticoid-induced skin atrophy in preclinical studies completed with mice [1]. Such agents can be added to a corticosteroid regimen to counteract the inhibition of collagen synthesis, preventing corticosteroid-induced effects [36]. By preventing steroid-induced skin atrophy, including skin-thinning, combination therapies are able to reduce major corticosteroid side effects that stand in the way of long-term use. Long-term use is often needed for successful treatment of diseases - combination therapies can decrease side effects, while also improving patient quality of life and overall skin health.

CONCLUSION

The pathophysiology of skin thinning due to corticosteroid use reveals complex interactions that disrupt skin integrity. The suppression of fibroblast activity, dysregulation of matrix metalloproteinases (MMPs), and the accumulation of oxidative stress all contribute to the degradation of the extracellular matrix (ECM), weakening the dermal structure and leading to increased skin fragility. Histological alterations occur early in corticosteroid therapy, often preceding visible signs of skin thinning, highlighting the importance of early

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detection through advanced imaging technologies such as high-frequency ultrasound (HFUS), elastography, and optical coherence tomography (OCT). These diagnostic tools allow for real-time monitoring of dermal changes, enabling timely interventions to prevent irreversible damage.

The relationship between glucocorticoid dose and adverse events, particularly skin thinning, underscores the need for careful management of corticosteroid therapy. Regular monitoring, along with dose adjustments, can mitigate the risk of skin-related complications. Additionally, therapeutic strategies focusing on restoring ECM balance, such as using growth factors and antioxidants, hold promise in counteracting the damaging effects of corticosteroids on skin elasticity. As diagnostic and therapeutic approaches continue to evolve, clinicians will be better equipped to prevent, detect, and manage corticosteroid-induced skin thinning, ultimately improving patient outcomes. This proactive approach ensures that the benefits of corticosteroid treatment are maximized while minimizing the impact on skin health.

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CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

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