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AN OVERVIEW ON VITAMIN D AND SKIN DISEASES

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ABSTRACT

Vitamin D, originally associated with rickets and osteocalcin, has recently been shown to have a role in a number of medical and dermatological diseases. It has been found that vitamin D receptors and the enzymatic machinery capable of converting circulating 25-hydroxyvitamin D [25(OH)D] to the active 1,25-hydroxyvitamin D [1,25(OH)D] is present in most cells in the body including the skin. It is well known that vitamin D analogs are effective in the treatment of psoriasis vulgaris because of their anti-proliferative and pro-differentiating effects on keratinocytes. However, new roles have been found for vitamin D in skin, such as immunomodulatory and anti-apoptotic effects thus raising a possibility of its use in conditions such as atopic dermatitis and infections. Increasing evidence now indicates that cutaneous vitamin D synthesis may help in prevention of skin malignancies and further, that cancer mortality may be reduced by oral supplementation of vitamin D. Various epidemiological studies have linked low levels of vitamin D to autoimmune diseases including vitiligo, and topical vitamin D has been used to treat vitiligo. This review focuses on a wide array of roles of vitamin D in various skin disorders with emphasis on both its well-established role as in psoriasis and the less characterized role in other disorders such as ichthyosis, tuberculosis or acne.

KEYWORDS: *Icthyosis, Psoriasis, Vitamin D, Skin Diseases, Vitiligo.*

1. INTRODUCTION

Vitamin D, commonly known as the sun exposure, has lately been linked to a number of health problems. The decrease in the prevalence of rickets after the fortification of foodstuffs with vitamin D led doctors to think that vitamin D-related health problems were no longer a problem(1). But, regrettably, rickets seems to be a drop in the ocean of diseases caused by vitamin D insufficiency. The main sources of vitamin D for people are enough sunshine and a diet rich in fatty fish and fortified milk(2). Vitamin D acts as a hormone, regulating parathyroid hormone (PTH), calcium, and phosphorous metabolism, all of which have significant consequences for bone health(3). The revelation of vitamin D receptors (VDRs) for most cells of the body, as well as enzymes that synthesize the active form of vitamin D, 1,25-dihydroxyvitamin D [1,25(OH) 2D], in non-renal sites like skin, has sparked renewed interest in its functions, particularly its role in lowering the risk of several chronic, highly morbid conditions like carcinomas and autoimmune diseases(4). Vitamin D's cutaneous production and involvement in the treatment of common skin diseases such as psoriasis has made it a hot subject among dermatologists(5). Studies pointing to vitamin D's function as an immunomodulator have paved the way for further research into its therapeutic benefits in atopic dermatitis, psoriasis, especially skin cancer(5).

1.1. The Cutaneous Biosynthesis Pathway of Vitamin D3:

Pro-vitamin D3 or 7-dehydrocholestrol, which is present mainly in the epidermis' basal and spinous cell layers, undergoes a photochemical reaction to produce pre-vitamin D3(2). Because melanin blocks UV light, dark skinned people need more UV light exposure to generate

comparable quantities of Vitamin D3(6). The human skin's vitamin D3 pathway. Calcitriol bound to vitamin D binding protein operates on certain additional target tissues that express vitamin D receptors, such as bone, gut, and parathyroid gland, via both genomic and non-genomic processes.

1.2. Effects on the immune system of the skin:

Several immune cells, including monocytes, T and B lymphocytes, and Langerhans cells, express both vitamin D receptor and 25-hydroxyvitamin D-1-hydroxylase, indicating that vitamin D plays an important role in immune modulation and regulation(7). Vitamin D's immunomodulatory properties. Apoptosis of keratinocytes is affected. Calcitriol stimulates ceramide production by activating the neutral Mg2+-dependent sphingomyelinase (thereby boosting sphingomyelin to ceramide conversion) and ceramide, in turn, increases calcitriol's pro-differentiating action on keratinocytes in a feedback loop. Physiological amounts of calcitriol inhibit the effects of pro-apoptotic ceramides, UV radiation, and tumor necrosis factor (TNF-)(8).

1.3. Antioxidant properties:

Vitamin D's photoprotection against damaging oxygen radicals produced by UVB radiation may be explained by the production of an antioxidant in keratinocytes in vitro.

1.4. Vitamin D's Impact On Skin Diseases:

1.4.1. The connection between vitamin D as well as psoriasis:

Despite the fact that topical vitamin D analogs have a well-established function in psoriasis, the exact processes behind their therapeutic efficacy are yet unknown(9). Following topical administration of vitamin D analogs, several indicators of epidermal proliferation, such as proliferating cell nuclear antigen (PCNA) and Ki-67 antigen, as well as differentiation (involucrin, transglutaminase K, filaggrin, or cytokeratins) were seen in situ in lesional psoriatic skin(10). Due to decreased absorption of topical preparations in the dermis, topical vitamin D does not assist much in decreasing dermal inflammation (cluster of differentiation (CD-) antigens, cytokines, HLA-DR, etc.) observed in psoriasis(10). Clinical improvement has been linked to increased vitamin D receptor mRNA in vitamin D–treated cutaneous lesions, resulting in the classification of "responders" and "non-responders," with the former exhibiting an increase in vitamin D receptor mRNA in treated skin regions. Individual vitamin D receptor gene allelic variants may also influence therapy response. In psoriasis patients, the A allele was shown to be more associated with the vitamin D receptor(11).

The FokI polymorphism has been linked to calcipotriol responsiveness. Other research, on the other hand, have shown that different vitamin D receptor genotypes are not linked to calcitriol clinical response(8). Studies on the blood levels of 1,25(OH)2 D or 25(OH)D in psoriatic patients have shown mixed findings, with some indicating that 1,25(OH)2 D levels are lower in individuals with evident psoriasis. Furthermore, the association of pustular psoriasis with hypocalcemia and psoriasis aggravation with chloroquin treatment (mediated by a decrease in 1,25(OH)2 D levels owing to inhibition of 1-(OH)ase (CYP27B1)) are well documented(12).

1.5. Atopic dermatitis or vitamin D:

Vitamin D supplementation is a viable therapeutic treatment for atopic dermatitis since it has the capacity to reduce inflammatory responses, improve antimicrobial peptide action, and maintain the integrity of the permeability barrier(12). Vitamin D's involvement in the development of atopic dermatitis is not well understood. There was no link between low dietary vitamin D and clinical disease severity ratings in a study of 138 Norwegian individuals with atopic dermatitis(13). Vitamin D supplementation had a non-significant effect in seasonal atopic dermatitis, according to a tiny pilot trial. A research found that a higher vitamin D consumption in childhood is linked to a higher incidence of atopic symptoms. Vitamin D's immunomodulatory effects have been linked to

the development of atopic dermatitis in many recent studies. It was discovered that the active form of vitamin D increased antimicrobial peptide expression and therefore avoided skin infections. There's a connection between vitamin D-mediated toll-like receptor activation, cathelicidin synthesis, as well as bacterial infection sensitivity(9).

1.6. Vitiligo and vitamin D:

Autoimmunity plays an essential part in the pathophysiology of vitiligo, as shown by the coexistence of vitiligo and other autoimmune diseases. As a result, vitamin D levels have been shown to be lower in a variety of autoimmune diseases, suggesting a link between vitiligo and vitamin D levels. The precise method by which vitamin D affects autoimmunity, however, remains a mystery(4).

1.7. Ichthyosis and vitamin D:

In the literature, there are many instances of a link between keratinization abnormalities and rickets. Calcitriol inhibits the growth of keratinocytes and aids in the mineralization of new bones by boosting calcium and phosphorus absorption from the gut. As a result, diseases like ichthyosis, which is characterized by aberrant keratinization, may be linked to a change in vitamin D metabolism, resulting in rickets and osteocalcin(14). Skin cancer and vitamin D The discovery of vitamin D receptor expression on both normal and cancerous cells sparked a study into the vitamin D-cancer connection. In the etiology of non-melanoma cutaneous carcinomas, ultraviolet radiation is a well-known culprit(15). Vitamin D, as previously stated, protects keratinocytes from UV exposure in vitro(10). Furthermore, the formation of cutaneous tumors in vitamin D receptor defective animals in response to carcinogens has led to the notion that chronically increased blood vitamin D levels protect against melanoma. Furthermore, adequate vitamin - D levels may lower the risk of solid organ tumors like those of the abdomen, liver, colorectum, gall bladder, pancreas, lung, breast, prostate, bladder, and kidney, while maintaining the risk of non-melanoma cutaneous cancers due to the common wavelengths required for vitamin D production and cutaneous photodamage(16). There's also a link between blood vitamin D levels and cancer severity, with greater vitamin D levels in stage I melanoma compared to stage IV tumors, according to research(7).

1.8. Vitamin D and Fibrosis of the Skin:

Vitamin D inhibits both normal skin fibroblasts or keloid fibroblasts, suggesting that it may have a therapeutic function in keloids(17). Because of its effects on immunoregulation, fibroblast proliferation, collagen synthesis, and endothelial cell function, topical vitamin D analogs are an established therapeutic method in morphoea and lichen sclerosusetatrophicus. Calcipotreine's positive impact on morphoea may be explained by its suppression of T lymphocytes, which results in lower IL-2 release(18).

1.9. Affective disorders and vitamin D:

There have been several reports linking vitamin D receptor polymorphisms to an increased risk of autoimmune diseases such as Hashimoto's thyroiditis, inflammatory bowel disease, Graves' disease, rheumatoid arthritis, systemic lupus erythematosus (SLE), primary biliary cirrhosis (PBC), autoimmune hepatitis, Addison's disease, vitiligo, celiac disease (MS)(19). However, the majority of these findings are based on in vitro and animal research, with only contradictory human evidence(20). Despite this, vitamin D supplementation for the treatment of autoimmune diseases has been suggested(6)(21).

1.10 New Vitamin D Analogs Are Being Evaluated New Vitamin D Analogs Are Being Evaluated:

Multiple clinical and laboratory research are ongoing to create novel vitamin D analogs with a better clinical profile, in light of the health advantages of vitamin D(22). (1) analogs with

predominant cutaneous metabolism and minimal toxicities; vitamin D analogs achieved by combining the 20-methyl alteration with biologically interesting artificial side chain subunits or 2-substituted calcitriols are especially promising; (2) analogs with predominant cutaneous localization and also no systemic toxicity; This may be accomplished by creating compounds with different affinities for vitamin D receptors and nuclear co-factors, such as the retinoid X receptor (RXR)(23).

1.11. In The Indian Context Of Itamin D In The Indian Context Of Vitamin D:

It is a widespread misconception in India that vitamin D deficiency is rare(24). Vitamin D insufficiency is seen in all age groups and both sexes throughout the nation, according to published statistics. When serum 25(OH)D levels reach 30 ng/ml, vitamin D insufficiency is suspected. In India, the majority of research have used this definition. Variables such as age, sex, pubertal state, latitude, season, race, and ethnicity may affect the blood concentration of 25(OH)D(11,13).

2. DISCUSSION

Finally, the specific connection between vitamin D and dermatology could be clearly discerned. On the one hand, our skin is a source of this essential vitamin; on the other hand, all available evidence indicates that it has a significant effect on the health of our skin and that its shortage is linked to a variety of dermatological disorders. Numerous variables are responsible for keeping it at optimal levels; therefore, sunny conditions are far from a guarantee of offering a ‘‘comfort zone" regarding the risk of vitamin insufficiency, a worry confirmed by several epidemiological studies conducted near the equator. Based on current evidence, it is evident that taking vitamin D supplements is the best way to achieve normal blood levels and prevent the negative consequences of vitamin D insufficiency. More study is required to decipher its complex links to dermatological diseases and provide precise standards and guidelines for supplementation. 800W.Z.

3. CONCLUSION

The “sunshine” vitamin is a popular subject that has gotten a lot of attention in recent decades, especially since a large part of the world's population is deficient in it. Vitamin D has long been known for its role in bone production, but new research suggests that it also affects the correct operation of virtually every organ in our body, including the brain, heart, muscles, immune system, and skin. As a result, its lack has been linked to a variety of illnesses, including cancer, autoimmune diseases, cardiovascular disease, and neurological problems.

Its role in the etiology of many dermatological disorders is no exception, and it has sparked a lot of interest in recent years. Vitamin D has been shown to have new roles in the skin, including immunomodulatory and anti-apoptotic characteristics, suggesting that it may be utilized to treat atopic dermatitis and infections. Increasing evidence indicates that cutaneous vitamin D production, as well as oral vitamin D supplementation, may help prevent skin malignancies and reduce cancer mortality. In many epidemiological studies, low vitamin D levels have been linked to autoimmune diseases like vitiligo, and topical vitamin D is used to treat vitiligo. Vitamin D's function in a range of skin disorders is examined in this research, with an emphasis on both its well-known role in psoriasis as well as its lesser-known role in ailments such as ichthyosis, tuberculosis, and acne.

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