

Skin and vitamin D: New aspects for dermatology

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Introduction

Vitamin D is a fat-soluble steroid hormone, traditionally known as the “sunshine” vitamin. It is obtained by photo exposure, diet or supplements and is crucial for human health. It is globally known for its importance in calcium homeostasis, bone health and antirachitic activity. In recent years, it has been known that synthesis, activity and metabolism of vitamin D is greatly linked to skin. Vitamin D has been recently implicated in a plethora of medical illnesses.¹

Dietary sources of vitamin D

Adequate sunlight, diet rich in oily fish and fortified milk are the major sources for humans. There are very few natural sources of vitamin D. Cod liver oil, beef liver, egg yolks, cheese, mackerel, salmon and tuna are the major sources. Many countries fortify juices, milk, yogurt and cereals with vitamin D.²

Vitamin D synthesis

Vitamin D occurs in two main forms: ergocalciferol (vitamin D₂) produced by plants and cholecalciferol (vitamin D₃) derived from animal-based foods. The major source of

vitamin D in humans is the cutaneous synthesis in the presence of sunlight.³

At the basal layer of epidermis, the cholesterol is converted to 7-dehydrocholesterol (pro-vitamin D₃), which is a photochemical transformation into the intermediate compound pre-vitamin D₃ due to ultraviolet B radiation (UV-B) (**Figure 1**).⁴ Cholecalciferol synthesized in the skin is then transferred to the circulatory system. The first activation step takes place in the hepatic cells i.e. 25-hydroxycholecalciferol – calcidiol [25(OH)D], which is the main form of vitamin circulating in the blood. The second step is carried out in the renal cells with production of 1 α , 25-dihydroxycholecalciferol – calcitriol [1,25(OH)₂D], which is the main active form of the vitamin.³

Role of Vitamin D in Skin

Vitamin D regulates keratinocyte proliferation and differentiation, control of angiogenesis, immune regulation and apoptosis. It also plays a crucial role in defense against opportunistic infections and epidermal barrier renewal.

The most recent literature reports highlight the immunomodulatory effect of this compound, including stimulating immune system cell differentiation and inhibiting the production of pro-inflammatory cytokines that contribute to the development and progression of inflammatory process in skin diseases. Because of the proven impact of vitamin D on numerous disorders and its multiple activities, it is important to explore its role in skin diseases.⁵

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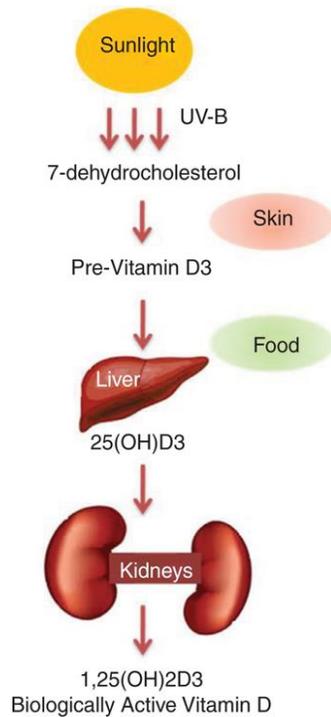


Figure 1 Biosynthetic pathway of vitamin D in humans, involving Sun exposure and hydroxylation by liver and kidney enzymes.⁴

Vitamin D and psoriasis

Psoriasis is a chronic immune-mediated inflammatory skin disorder which affects about 2-3% of the world's population.⁵ A correlation between low levels of serum vitamin D and increased severity of psoriasis has also been documented in the literature. Furthermore, improvement of psoriasis with sun exposure initiated the oral use of 1,25-dihydroxyvitamin D as a therapeutic option. The anti-inflammatory and anti-angiogenic activity of calcitriol counteract with inflammation and angiogenesis which is a feature of psoriatic lesion. It suppresses the pro-inflammatory Th1 and Th17 cell proliferation, as well as it induces regulatory T cells.¹

Vitamin D and vitiligo

Vitiligo is an acquired disorder of pigmentation which presents as hypopigmented patches due to

loss of melanocyte activity and destruction of epidermal melanocytes.⁵ Autoimmunity plays a key role in pathogenesis of vitiligo, vitamin D levels were found low in many autoimmune diseases, thus suggesting an association between vitamin D and vitiligo.¹

The antiapoptotic effect of vitamin D, controls activation, proliferation and migration of melanocytes thus promoting melanogenesis and tyrosinase content of human melanocytes. Vitamin D also plays a very significant role in decreasing autoimmune damage to melanocytes by T-cells. Topical vitamin D analogs have been effectively used in the treatment of vitiligo. In a study combined topical treatment with calcipotriol ointment and betamethasone ointment was shown to be less irritating and slightly more effective than calcipotriol used alone.⁶

Vitamin D and atopic dermatitis

Atopic dermatitis (AD) is a recurrent, chronic inflammatory skin disorder with a multifaceted pathogenesis involving an interplay of immunological imbalance and skin barrier deficiency. Since Vitamin D has immunomodulatory properties and enhance the integrity of cutaneous barrier, it is likely that vitamin D plays a role in AD.⁷ Researches have lately discovered that vitamin D supplementation improves the clinical course of AD. However, this specific mechanism is not clear. Many epidemiological studies have demonstrated that vitamin D supplementation may have a therapeutic role in this disease with a good safety profile.¹

Vitamin D in acne vulgaris

Acne vulgaris is a common, chronic inflammatory disorder of the hair-sebaceous unit.

Vitamin D counteracts the development and maintenance of inflammation and it inhibits excessive cell proliferation and regulates keratinocytes apoptosis. It also regulates local sebocytes' proliferation, lipid composition, secretion of IL-6 and IL-8. Moreover, sebocytes also express VDRs on their cell membranes. There are very few researches to establish the role of vitamin D as a treatment option. Currently, efficacy of topical calcipotriene as a therapy for acne, is under trial.⁵

Vitamin D and cutaneous malignancies

There is no direct evidence which proves a protective effect of vitamin D against melanoma and non-melanoma skin cancer. Moreover, in vitro studies revealed that vitamin D shows photoprotective effects by diminishing DNA damage, reducing apoptosis, increasing cell survival and decreasing erythema. The literature however provides conflicting results and lately, they found that vitamin D serum levels seem to be inversely associated with cutaneous melanoma Breslow thickness at diagnosis.⁵

Other cutaneous disorders

Studies have identified vitamin D deficiency in many cases of cutaneous lupus, systemic sclerosis, rheumatoid arthritis, Grave's disease, inflammatory bowel disease, autoimmune hepatitis, type I diabetes mellitus and multiple sclerosis. Therefore, monitoring and correcting the vitamin D status should be recommended in these patients.

Vitamin D deficiency has also been reported in patients with alopecia areata, mycosis fungoides, inherited ichthyosis, bacterial vaginosis and cutaneous tuberculosis. Patients with polymorphic light eruption (PLE), have decreased serum levels of 25-hydroxyvitamin-D₃ and correcting its level may ameliorate PLE.

On the other hand, topical calcitriol has also shown betterment in many skin conditions.^{1,7}

Conclusion

Role of vitamin D in skin is gaining momentum as this vitamin not only plays an important role in skin biology but also modulates inflammation, cytokine secretion and lymphocyte functioning. It therefore comes as no surprise that low levels of vitamin D have been associated with multiple dermatological disorders. Further trials involving larger sample sizes and longer treatment periods will be necessary to assess the true role of vitamin D as a therapeutic option in dermatologic diseases.

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