Role of Vitamin D in Keloid Disorder

Charlie Frankel*

Editorial Office, Plastic Surgery: Case Studies, Belgium

Corresponding Author*

Charlie Frankel

Editorial Office, Plastic Surgery: Case Studies, Belgium

E-mail: plastsurgery@eventsupporting.org

Received: 14 Feb, 2022, Manuscript No. PSCS-22-55040; **Editor Assigned:** 17 Feb 2022, PreQC No. PSCS-22-55040 (PQ); **Reviewed:** 21 Feb 2022, QC No. PSCS-22-55040; **Revised:** 24 Feb 2022, Manuscript No. PSCS-22-55040 (R); **Published:** 28 Feb 2022, DOI: 10.37532/pscs.22.3.1.1-2

Introduction

Vitamin D (VD) comes in two forms in the body: vitamin D2 (ergocalciferol, VD2) and vitamin D3 (cholecalciferol, VD3) (cholecalciferol, VD3). VD3 synthesis is influenced by ultraviolet B intensity, which varies depending on latitude, and skin pigmentation, which is determined by melanin. Because their metabolically active forms, 1, 25-dihydroxyvitamin D3 (1, 25$(OH)_2D_3$) and 1, 25-dihydroxyvitamin D2 (1, 25$(OH)_2D_2$), exhibit comparable physiologic activity when bound to VDR, both VD2 and VD3 shall be referred to as VD in this article. Vitamin D is well recognized for maintaining calcium and phosphorus homeostasis by signaling intestinal calcium and phosphate absorption to maintain calcium and skeletal balance through fast non-genomic effects. VDR inhibits cellular proliferation, stimulates differentiation, and inhibits adaptive immunity while increasing innate immunity by activating or inhibiting gene expression.

Vitamin D is converted to its physiologically active form in two steps: first, it is 25-hydroxylated in the liver to generate 25-hydroxyvitamin D (25OHD), which is subsequently 1,25-dihydroxylated by CYP27B1 to form 1,25-dihydroxyvitamin D (1,25$(OH)_2D$). Although the latter reaction takes place largely in the proximal renal tubule, this enzyme may also be present in non-renal tissues such as T and B cells. Because KALTs are made up of lymphoid aggregates, CYP27B1 may be present. Vitamin D's physiological effects are mediated by both genomic and non-genomic mechanisms. It binds to VDR, a DNA-binding transcription factor from the nuclear receptor superfamily of steroid hormones. VD binds to VDR, forming an active signal transduction complex with VD liganded to VDR and the retinoid X (RXR). Thousands of VDREs and hundreds of genes harboring VDREs have been found, indicating that the VDR-RXR heterodimer may identify VDREs on VD regulated genes and have genomic effects. Lymphocytes inside KALTs may express CYP27B1, resulting in local synthesis of VD, which might subsequently have genomic consequences *via* VDR signaling on ESC-like cells expressing VDR within KALTs. The presence of CYP27B1 in lymphocytes within the KALTs should be investigated further.

Vitamin D deficiency in keloid disorder

KD patients are more prone to have VD Deficiency (VDD), hypertension, and dark skin. Dark-skinned people are also more likely to have VDD and hypertension. Sunlight exposure is the major source of VD, with skin pigmentation being a crucial driver in lower UVB penetration, resulting in decreased cutaneous VD3 production. Individuals with very dark skin, such as those found in some African communities, may have a sun protection factor of up to 15, which absorbs up to 99% of UVB light and, as a result, reduces VD3 production by up to 99%, increasing vulnerability to VDD. Keloid fibroblasts show a dose-dependent reduction in proliferation in response to VD3 therapy, with collagen I expression dropping thrice in the treated samples, indicating that VD3 has an effect on keloid regression. TGF-β1/Smad signaling is negatively regulated by the vitamin D receptor. In patients with systemic sclerosis, VDR suppression increases fibroblast sensitivity to TGF-β1, and activation of VDR with paricalcitol lowers TGF-β1's stimulatory action on fibroblasts, inhibiting collagen synthesis and myofibroblast differentiation. In addition, paricalcitol promotes the creation of VDR and phosphorylated Smad3 complexes, which inhibits Smad transcriptional activity, which controls the production of profibrotic genes such as MMPs, proteoglycans, integrin, and plasminogen activator. The susceptibility genes for KD have been identified as plasminogen activator and VDR.

VDR expression is considerably reduced in KD patient's peripheral blood cells, KL epidermis, and fibroblasts from patients with systemic sclerosis, another fibrotic illness. We recently shown that the ESC-like population within the KALTs also expresses VDR, as well as RAS components and cathepsins B, D, and G, which are RAS bypass loops. VD's genomic effects upon binding to VDR may control gene expression regulating EMT, endo-MT, and subsequent cellular differentiation and proliferation, and hence may contribute to the production of keloid fibroblasts and myofibroblasts via a mesenchymal stem cell intermediate in KD. More research is needed to see if VDD affects the proliferation and development of ESC-like cells throughout the body. The fact that darker skinned people are more prone to VDD, hypertension, and KD may provide insight into the disease's pathophysiology. The anti-proliferative impact of VD, as seen by reduced Bcl-2 and increased caspase-3 expression, suppression of TGF-β1/Smad signaling, and possible effect on ESC-like cells inside KALTs, highlight the need for further research that might lead to VD supplement treatment for KD.

Immune system and vitamin D in keloid disorder

VD impacts cells in larger proportions in KLs than in normal skin, and significant VDR transcripts are identified inside IL-17 generating TH17 cells, suggesting that VDR may play a role in the IL-6/IL-17 axis, which regulates primitive cells in KLs. Furthermore, because KD contains autoimmune features that may be mediated by autoimmune responses, immunological effects generated by VD may have an impact on the immune response observed in KD, eventually influencing the keloid micro environmental niche, and therefore potentially the ESC-like cells on KALTs. Vitamin D may have auto-immune protective effects on the micro environmental niche within KLs, causing the ESC-like population within the KALTs to behave differently. Pathological scarring in KD is characterized by activation of the NF-kB pathway, its limited attenuation in VDD, and enhanced fibroblast proliferation and ECM synthesis mediated by RAS activation. Treatment for KD remains empirical and unsatisfactory despite much study. A growing body of data implies that an ESC-like population plays a critical role in KALTs. The proliferation and accumulation of keloid fibroblasts and myofibroblasts can be regulated by a micro environmental niche centered on the RAS, including its bypass loops made up of enzymes like cathepsins B, D, and G, as well as converging signaling pathways like VDR-mediated mechanisms and the immune system. The complicated interplay between the RAS, VDR, other chemicals, and the immune system, which together comprise the micro environmental niche, may lead to innovative targeted therapeutics for this puzzling and difficult condition.

Cite this article: Frankel C. Role of Vitamin D in Keloid Disorder. Plast Surg: Case Studies. 2022, 3 (1), 001.